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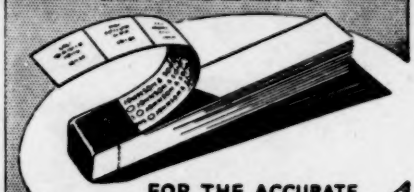

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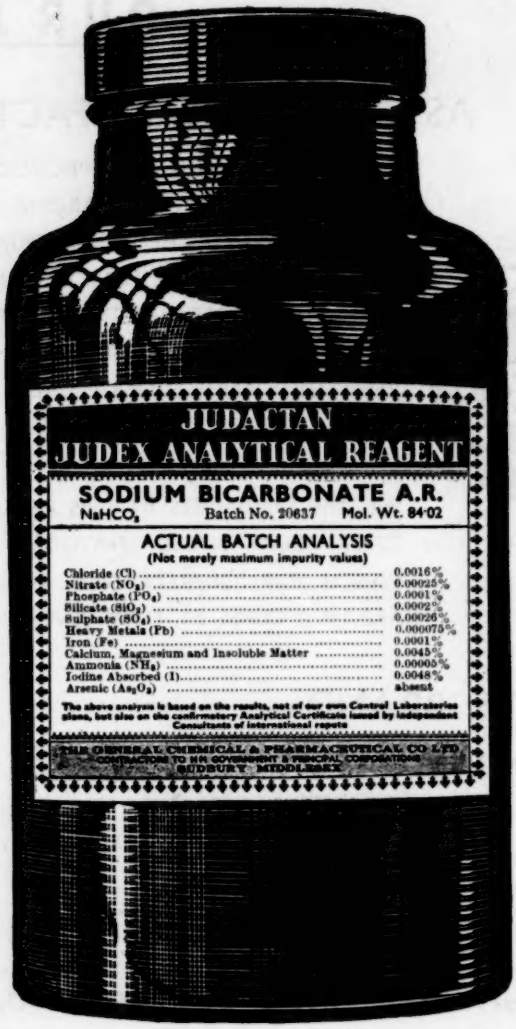
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286. *The Hydrothermal Chemistry of Silicates. Part II.* Synthetic Crystalline Sodium Aluminosilicates.*

By R. M. Barrer and E. A. D. White.

The hydrothermal reactions of sodium aluminosilicate gels have been investigated between 150° and 450°. Crystal growth has been examined in absence and in presence of additional sodium compounds (NaCl, Na_2SO_4, Na_2CO_3, and NaOH) in the mother-liquors. Gel compositions were in the range $Na_2O,Al_2O_3,1—12SiO_2$.

The conditions employed gave rise to a felspar (albite); zeolites (analcite and mordenite); a mica (paragonite); felspathoids (nepheline, sodalite, nosean, and cancrinite), and α-quartz. Two hydrated phases of nepheline composition were synthesised, and also a range of crystalline phases related to the cancrinite, nosean, and sodalite structures, but without the usual interstitial salts. Rather large laminar crystals, of an apparently new hydrated silicate species, were formed in some preparations, and also large crystals of sodium silicate. Details of two new species obtained in minor yields are recorded.

All the compounds have been characterised by optical and *X*-ray methods, which in some cases reveal interesting differences between synthetic and naturally occurring forms of the mineral. Some ion-exchange reactions of cancrinite, nosean, and sodalite-type minerals, one of the minerals of nepheline composition, and one of the minor species were studied.

Despite the technical and scientific interest of many naturally occurring aluminosilicates, problems relating to their reproducible laboratory synthesis and their properties have as yet been solved very incompletely. The chemistry of mineral reactions can usually be inferred only in general outline from geochemical reasoning. Much of the earlier literature of hydrothermal reactions has been summarised by Morey and Ingerson (*Econ. Geol.*, 1937, **32**, 607), and Barrer (*Faraday Soc. Discussion*, 1949, **5**, 326) has discussed the principal synthetic methods in silicate mineral chemistry.

Recently, by direct synthesis from gels under carefully specified conditions, much new information on mineral formation has been obtained in this laboratory (Barrer, *J.*, 1948, 2158; 1950, 2342; H. W. Taylor, *J.*, 1949, 1253; Barrer and White, *J.*, 1951, 1167) and also by continental and American workers (Noll, *Neues Jahrb. Min.*, Beil. Bd., 1935, **70**, 65; Wyart, *Discuss. Faraday Soc.*, 1949, **5**, 323; Roy, Roy, and Osborne, *J. Amer. Ceram. Soc.*, 1950, **33**, 152; Friedman, *J. Geol.*, 1951, **59**, 19). In particular, Noll has been concerned with mixtures in which the ratio base : alumina in the parent aluminosilicate gel is varied and is usually less than unity, while the alumina : silica ratios are fixed in a few proportions only. Clay formation was one hydrothermal reaction in such mixtures (giving, for example, kaolinite, pyrophyllite, and montmorillonite). On the other hand, in the authors' work with the molar ratio base : alumina equal to or (by addition of excess alkali) rather greater than unity, and with systematic variation of the silica content, conditions were more alkaline. The compositions then crystallised as zeolites, felspars, felspathoids, quartz, and other species. In the present paper are given some new results obtained with gels $Na_2O,Al_2O_3,nSiO_2,aq.$ ($n = 1—12$), which completes an earlier investigation where $8 < n < 12$ (Barrer, *J.*, 1948, 2158; *Nature*, 1946, **157**, 734) and which showed conditions necessary for the formation of analcite, mordenite, quartz, and other crystals.

The system $Na_2O–Al_2O_3–SiO_2$ has been investigated by other workers using pyrolytic and hydrothermal methods. Recently Friedman (*loc. cit.*) investigated part of this system hydrothermally and under rather specialised conditions. He obtained much information but few synthetic products.

Wyart (*loc. cit.*) has described crystallisations from the gels $Na_xK_{1-x}AlSiO_4$ ($0 < x < 1$), running from kaliophilite to nepheline in composition. Species reported included

* Part I, *J.*, 1951, 1267.

nepheline, cancrinite, and a sodalite-type mineral. Little information is given about these products, but it seems likely that they would prove similar to corresponding species reported in this paper.

Experimental

The apparatus and methods used were described in Part I (*loc. cit.*). Gels of composition $Na_2O,Al_2O_3,nSiO_2,mH_2O$, in which n varied from 1 to 12, were prepared by mixing the constituents in the necessary proportions when in aqueous suspension or solution. The mixtures were evaporated under various conditions (*e.g.*, over a steam-bath or in an air-oven at temperatures up to 120°), to creamy consistency and through intermediate stages up to dry gels.

The examination of the products of subsequent hydrothermal treatment of these gels has already been described (Part I). The larger size of many of the sodium aluminosilicate crystals now obtained enabled additional data to be determined from single crystal *X*-ray photographs, taken with a Unicam camera.

Results

Products from gels of composition $Na_2O,Al_2O_3,nSiO_2$, treated hydrothermally at temperatures between 150° and 450°, are shown in Table 1. In many cases the addition of $\geqslant$100% excess of sodium hydroxide (in molar proportion) resulted in the formation of different minerals under otherwise similar experimental conditions. A slight excess only of sodium hydroxide enhanced the ease of crystallisation of the gels in almost all cases. Products in the same field, but grown in the presence of excess alkali hydroxide, are given in parentheses in Table 1.

Experiments were also made in which excess of sodium chloride, sulphate, or carbonate was added to the reaction mixtures. It was found that the products over almost the whole of the conditions of composition, pH, and temperature recorded in Table 1 were sodalite and nosean in the presence of chloride and sulphate respectively. In high-silica mixtures some albite and analcite were also observed. With insufficient added salt, a limited amount of sodalite or nosean was formed, together with crystals normally formed in that region in absence of added salts. The addition of sodium carbonate did not result in marked alteration of the usual products, but extended the conditions of formation of cancrinite (*i.e.*, formation at lower temperatures was observed), and improved the crystallisation of other appropriate species.

Crystallisation was more difficult from gels dried under rigorous conditions (*e.g.*, evaporated to dryness at 120° before hydrothermal treatment). Optimum crystallisation usually occurred when gels were evaporated to the consistency of a thick cream on the steam-bath. The effect of drying the gels was, however, counteracted when much alkali hydroxide was present in the mineralising mother-liquor, or when hydrothermal crystallisation was conducted at higher temperatures (>350°).

One may comment on the dominance of the zeolitic phase analcite over much of the field explored, although at higher temperatures albite (from high-silica gels) and paragonite (from low-silica gels) become dominant. At moderate temperatures the yield of analcite increased sharply at $n = 4$ with rising silica content of the gel $Na_2O,Al_2O_3,nSiO_2$, and then decreased slowly for still higher values of n. At temperatures approaching 300°, with increasing values of n small yields of mordenite appeared in the products, the yield rising to a maximum at $n = 10$. Some quartz was also formed in this region, and in increasing yield as n increased further (Barrer, *Nature*, 1946, **157**, 734). The addition of sodium carbonate in the high-silica region facilitated crystallisation of mordenite and quartz, but when the mother-liquor became very alkaline the initial precipitate of mordenite was attacked and recrystallised (cf. Barrer, *J.*, 1948, 2158).

Fig. 1, *a*—*g*, shows diagrammatically the regions of temperature and composition over which some important species were obtained, first at lower pH and then under highly alkaline conditions. Very high pH ($\geqslant$100% molar excess of sodium hydroxide) did not greatly influence the formation of the low-temperature phases. Above 300°, however, several new species appeared. From gels $Na_2O,Al_2O_3,2SiO_2$ + NaOH,aq. at 450°, progressive increasing of pH gave, successively and in nearly 100% yields, paragonite, large nepheline crystals, cancrinite, and finally nosean-type phases. Moreover, at temperatures between 300° and 400° and over restricted ranges of composition (Fig. 1*f*) three new crystal species were grown. Two of them have the composition of nepheline, and since they are hydrated they are here designated as nepheline hydrates I and II. The third species (compound L) grew as plates up to 5 mm. across, but was not identified with any natural mineral. In general, these crystals were secondary products, although yields approaching 100% were occasionally noted.

TABLE 1. *Summary of results of crystallisation of gel compositions* $Na_2O,Al_2O_3,nSiO_2$.*

Temp.	$n = 1$	$n = 2$	$n = 3$	$n = 4$	$n = 5$
150°	V. poor F 10·0 (Poor F)	Poor F & B 10·0 (Poor F & B)	Poor F, some B 10·0 (Poor F & B)	Poor B 10·0 (Good B)	V. poor B 10·0 (Good B)
180	V. poor F 10·5 (Poor F & B)	V. poor F 9·3 (Poor F & B)	V. poor F & B 9·0 (Poor B & F)	Poor B 10·0 (V. good B)	Poor B 9·3 (V good B)
210	V. poor F 10·0 (Mod. B & F)	Poor F 9·7 (Mod. B & F)	Poor F & B 9·3 (Good B)	Good B 9·0 (V good B)	Good B 9·3 (V. good B)
240	Mod. F & B 8·3 (Mod. B, some I)	Mod. F & B 8·7 (Mod. B, some I)	Mod. F & B 8·7 (Mod. B, some I)	V. good B 8·3 (V. good B)	V. good B 8·0 (V. good B)
270	Some F 8·7 (Mod. B, some J)	Mod. F, some B 8·7 (Mod. B, some J)	Mod. B, some F 9·0 (Mod. B, some J)	V good B 8·0 (Good B)	Good B 7·7 (Good B)
300	Some F 9·0 (Mod. F)	Mod, F, some B 9·4 (Mod. F, some J)	Mod. B 7·4 (Mod. F, some B)	Good B 7·4 (Mod. B, some A)	Good B 7·4 (Mod. B & A)
330	Some F 9·4 (Mod. F & I)	Mod. F, some I 9·7 (Mod. F & I)	Some F & I 9·0 (Mod. F, some B)	Mod. B 8·4 (Mod. B & A)	Mod. B 8·4 (Mod. A)
360	Poor G 7·4 (Good E & J)	Some G & B 8·3 (Good E, some J)	Poor B & G 8·0 (Mod. E, some J)	Mod. B, some C 8·4 (Good A, some B)	Mod. A, some B 7·7 (Mod. A & B)
390	Mod. G 7·4 (Mod. E)	Mod. G, some B 8·0 (Good K, some E)	Poor G 7·7 (Good K, some E)	Poor G, some B 7·4 (Mod. E & B)	Poor A 7·7 (Mod. B & A)
420	Good G 7·7 (Good E)	Good G 7·4 (V. good E)	Mod. G 7·7 (V. good E)	Poor G, some B 7·4 (Good E)	Poor G, some A 7·7 (Good B & A)
450	V. good G 7·4 (V. good E)	Good G 7·4 (V. good E)	Mod. G 7·4 (V. good E)	Mod. G 7·0 (V. good E)	Poor G 7·4 (Mod. E & A)
	$n = 6$	$n = 7$	$n = 8$	$n = 9$	$n = 10$
150	−10·0 (Good B)	−10·0 (Good B)	−10·0 (Good B)	−10·0 (Mod. B)	−10·0 (Mod. B)
180	Poor B 10·5 (V. good B)	Poor B 9·0 (V. good B)	Poor B 9·0 (Good B)	V poor B 9·0 (Good B)	V. poor B 10·0 (Mod. B)
210	Mod. B 9·7 (V. good B)	Mod. B 9·3 (V. good B)	Mod. B 9·7 (V. good B)	Mod. B, some D 10·0 (Good B)	Mod. B & D 9·0 (Good B)
240	Good B 8·3 (V good B)	Good B, some D 8·7 (V. good B)	Good B, some D 9·0 (V. good B)	Mod. B & D 9·0 (Good B)	Mod. D, some B 8·7 (Good B)
270	Good B 8·0 (Good B)	Good B 8·0 (Good B)	Good B, some D 7·7 (Good B)	Mod. D, some B 8·0 (Good B)	Good D 8·3 (Mod. B)
300	Good B 9·0 (Mod. B & A)	Good B 7·4 (Mod. B & A)	Mod. B & D 7·4 (Mod. B & A)	Good D, some B 7·4 (Mod. B & A)	V. good D, some B & H 8·0 (Poor B & A)
330	Mod. B, some A 8·0 (Good A)	Mod. B, some A 8·0 (Good A)	Mod. B, some D 7·7 (Good A)	Poor D & B 7·7 (Good A)	Mod. D 8·0 (Mod. A)
360	Mod. A 8·0 (Good A & B, some N)	Mod. A 8·4 (Good A, some B & N)	Mod. A 8·4 (Good A, some N)	Mod. A 8·4 (Good A)	Some A 8·7 (Good A)
390	Good A 8·4 (V. good A, some N)	Good A 8·0 (Good A, some N)	Mod. A 7·7 (Good A)	Mod. A 7·7 (Good A)	Poor A 7·4 (Good A)
420	Good A 8·0 (Good A, some B)	Good A 7·7 (Good A)	Good A 7·7 (Good A)	Mod. A 7·7 (Good A)	Mod. A 7·4 (Mod. A)
450	Poor G & A 7·7 (Good A)	Some G & A 7·7 (Good A, some B)	Poor A 7·4 (Good A)	Poor A 7·4 (Good A)	Some A 8·0 (Mod. A, some B)

* For significance of letters, see Table 2.

Note: Results in parentheses refer to growth in NaOH aq. (≤100% molar proportion). Figures refer to pH of cold mother-liquors.

TABLE 2.

Name	Ref. letter (Table 1)	Ideal empirical formula
Albite	A	$Na_2O,Al_2O_3,6SiO_2$
Analcite	B	$Na_2O,Al_2O_3,4SiO_2,2H_2O$
Cancrinite	C	$3(Na_2O,Al_2O_3,2SiO_2),Na_2CO_3$
Mordenite	D	$Na_2O,Al_2O_3,10SiO_2,6{\cdot}7H_2O$
Nepheline	E	$Na_2O,Al_2O_3,2SiO_2$
Nosean	F	$3(Na_2O,Al_2O_3,2SiO_2),Na_2SO_4$
Paragonite	G	$Na_2O,3Al_2O_3,6SiO_2,2H_2O$
Quartz	H	SiO_2
Sodalite	I	$3(Na_2O,Al_2O_3,2SiO_2),2NaCl$
Nepheline hydrate I	J	No natural counterpart, $Na_2O,Al_2O_3,2SiO_2,H_2O$
Nepheline hydrate II	K	,, ,, $Na_2O,Al_2O_3,2SiO_2,\frac{1}{4}H_2O$
Compound L	L	,, ,, $2Na_2O,Al_2O_3,6SiO_2,2H_2O$
Compound M	M	,, ,,
Compound N	N	,, ,,
Sodium silicate	O	Na_2O,SiO_2

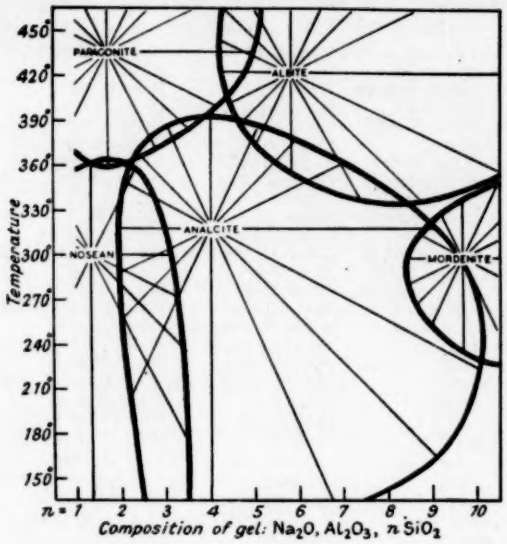
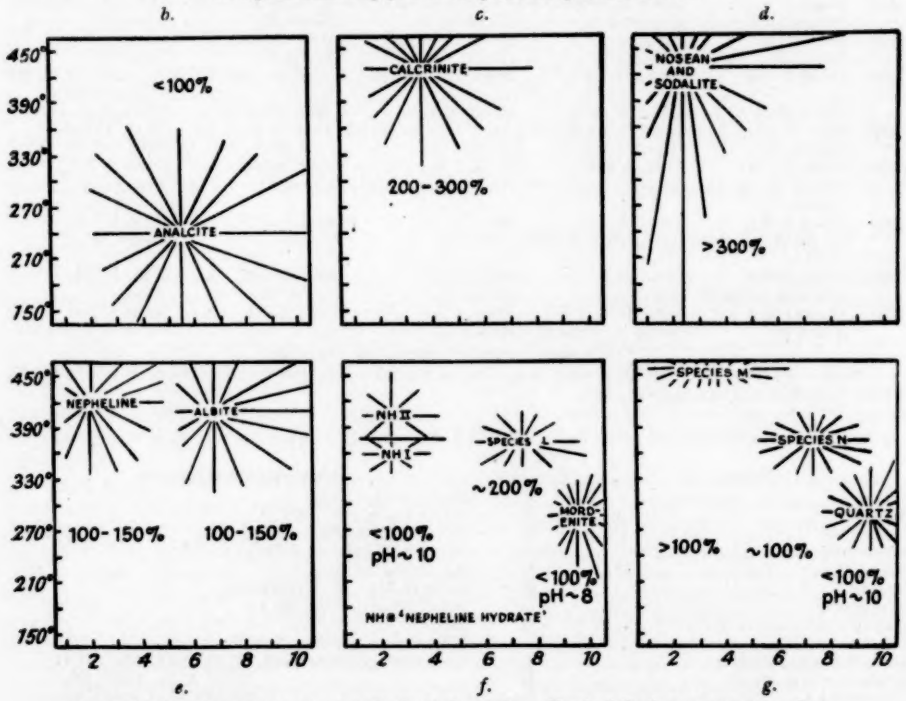


FIG. 1a. *Diagrammatic representation of the approximate areas of formation of the products obtained by crystallisation of the gels:* $Na_2O,Al_2O_3,nSiO_2 + aq.$ *(no excess* NaOH *added).*

The curves do not represent rigid boundaries; considerable overlapping of the products occurs. The mineral names are approximately located in the area where optimum formation occurs.

FIGS. 1b—g. *Digrammatic representation of the approximate areas of formation of products obtained by the crystallisation of gels in the presence of excess* NaOH.



Horizontal Scale: values of n *for* $Na_2O,Al_2O_3,nSiO_2$. *Vertical Scale: temperature* (° C).
Percentages refer to amounts of NaOH *added in excess of gel composition.*

The principal species synthesised are given in Table 2 and some of their properties will now be described.

Zeolites.—The zeolites analcite and mordenite were readily obtained, analcite in 100% yield and mordenite often in major, but not 100% yield, from gels of their own composition.

Analcite was prepared in three habits: as spherulites, as ikositetrahedra, and as cubes with hemihedral faces (Plate I). The maximum crystal dimension was 0·5 mm., but more usually the crystals were much smaller (20—50 μ). It was possible to obtain 100% yields whether in 1-g. or 5-kg. quantities (Barrer, *Faraday Soc. Discussion*, 1949, **5**, 326). The crystals were isotropic and with unit-cell cube edge of 13·67 Å. The sorptive and ion-exchange properties of analcite have been studied elsewhere (Barrer, *Proc. Roy. Soc.*, 1938, *A*, **167**, 392, 406; Barrer and Ibbitson, *Trans. Faraday Soc.*, 1944, **40**, 195; Barrer, *J.*, 1950, 2342).

Mordenite grew as thin laths, usually in wheatsheaf-like clusters, up to ~25 μ in length. The crystals were weakly birefringent with a mean R.I. = 1·467, and were monoclinic. The conditions of growth of mordenite and its ion-exchange reactions have been described rather fully elsewhere (Barrer, *J.*, 1948, 2158). The temperature range of formation has been extended in the present work (Fig. 1*a*), as has the range of interchangeable cations which now includes the series Li^+, Na^+, K^+, Cs^+, Ag^+, NH_4^+, Tl^+, Ca^{++}, and Ba^{++}. The sorptive and molecular-sieve properties of dehydrated mordenite are noteworthy (Barrer, *Trans. Faraday Soc.*, 1944, **40**, 555; *Quart. Reviews*, 1949, III, 293), and various ion-exchanged forms show the same type of sorptive behaviour as the parent mineral, modified to varying degrees by the cations present.

Hydrated Non-zeolitic Species.—Three hydrated, non-zeolitic phases were obtained: nepheline hydrate I, nepheline hydrate II, and compound L (Table 2).

Nepheline hydrate I (Plates II and III) occurred as complex hexagonal tablets, almost without exception showing mimetic twinning. Maximum dimensions were 150 μ. The optimum growth was observed at ~360° from gels $Na_2O,Al_2O_3,2—3SiO_2$ at pH values of ~10 (*i.e.*, slight excess of sodium hydroxide). It was usually a secondary phase to analcite, but yields approaching 100% were also obtained. The region of formation is comparatively restricted (Fig. 1*f*). The crystals showed moderate birefringence and straight extinction and belonged to the orthorhombic system, with $\alpha = 1·503$, $\beta = 1·506$, and $\gamma = 1·508$. Analysis gave a formula close to $Na_2O,Al_2O_3,2SiO_2,H_2O$. Dehydration of the crystals did not render them capable of sorbing ammonia. The compound may be the "hydronephelite" prepared by Thugutt (*Z. anorg. Chem.*, 1892, **2**, 64, 113) but he did not give identifying physical data.

Nepheline hydrate II (Plate IV) occurred as twinned hexagonal plates in a restricted region indicated in Fig. 1*f*. It grew best from gels $Na_2O,Al_2O_3,2SiO_2$ at ~420° in the presence of a slight excess of sodium hydroxide (pH ~10). These crystals were identical in appearance with the twinned hexagonal plates of nepheline hydrate I (Plate III), but were of higher refractive index ($\alpha = 1·548$, $\beta = 1·546$, $\gamma = 1·534$). They also showed straight extinction and belonged to the orthorhombic system. The maximum diameter of the hexagonal plates was ~250 μ. This species was found in close association with nepheline. For example, Plate IV shows typical crystals of nepheline hydrate II, from the centres of which protrude hexagonal prisms of nepheline. The moisture content was lower than for nepheline hydrate I, and a nepheline composition being assumed, it corresponded nearly to $Na_2O,Al_2O_3,2SiO_2,\frac{1}{2}H_2O$. *X*-Ray powder photographs of the two hydrates (Table 6) showed no particular resemblance either *inter se* or with nepheline. Nevertheless, there may be some structural similarities: nepheline hydrate II and nepheline must have a lattice arrangement along the 001 plane similar enough to permit overgrowth; the refractive indices along the *c* axes are identical.

Compound L (Plate IV) was obtained in moderate yield from gels $Na_2O,Al_2O_3,6—10SiO_2$ at 350° in presence of a large excess of sodium hydroxide (~300%). The crystals grew as tablets up to 5 mm. in length and could easily be separated by hand-picking or sieving. They were usually a secondary phase, and conditions of formation were restricted (Fig. 1*f*) although they were reproducibly formed. The crystals were obtained as irregular hexagonal tablets, easily cleavable into thin sheets. They were of low birefringence, biaxial positive, with a mean R.I. = 1·49; they belong to the monoclinic system having a unit cell of $a = 8·10$, $b = 6·10$, $c = 4·88$ Å, $\beta = 105°\ 20'$. Great resistance to attack by concentrated acids was shown, and on ignition the crystals readily fused to a glass with 7% loss in weight. On dehydration *in vacuo* they showed no sorptive power towards ammonia. *X*-Ray spacings are given in Table 6.

Nepheline hydrates I and II and compound L appear to have no natural counterparts, although the last shows similarities to the mineral ussingite ($2Na_2O,Al_2O_3,6SiO_2,H_2O$). Analysis of hand-picked crystals showed compound L to have composition close to $2Na_2O,Al_2O_3,6SiO_2,2H_2O$. Refractive indices of the two compounds are also similar (for

ussingite, $n \sim 1{\cdot}50$) but the *X*-ray powder-diffraction patterns of the two materials are not related.

Micaceous Products.—The only mica obtained was paragonite, which formed from gels $Na_2O,Al_2O_3,2SiO_2$, aq. at 420° and at low pH (~7). Yields approached 90% and the product comprised very small anhedral crystals (~5 μ) present in masses. The crystals showed high birefringence with maximum and minimum R.I. of 1·579 and 1·573. Natural paragonite is of rather rare geochemical occurrence.

Albite. The felspar albite was obtained in two characteristic habits (Plate V). Optimum growth occurred from gels of albite composition at 420° and at pH ~10 (the pH was not critical, however). The crystals, up to 50 μ in length, were frequently twinned, monoclinic, of low birefringence, and in some orientations gave oblique extinction; $\alpha = 1{\cdot}529$, $\beta = 1{\cdot}532$, $\gamma = 1{\cdot}537$.

Some differences from the natural compound were observed from the *X*-ray powder photographs (Table 6), but identity was apparent with albite obtained by ignition from synthetic analcite (Table 4), and it is probably the high-temperature modification of albite (Tuttle and Bowen, *J. Geol.*, 1950, **58**, 572; Friedman, *ibid.*, 1951, **59**, 19).

Felspathoids. Felspathoids obtained were nepheline, cancrinite, nosean, and sodalite. Excellent growth was observed in all cases from gels $Na_2O,Al_2O_3,2SiO_2$ in the presence of varying quantities of excess of sodium hydroxide (see Figs. 1*b*—*g*).

Nepheline (Plate VI) was usually formed as elongated hexagonal prisms with pyramidal ends, terminated by basal pinacoids, but occasionally it occurred as thick hexagonal tablets. The larger crystals were 1—2 mm. in length, and under crossed Nicols showed a cross-hatched structure, presumably due to complex twinning. Best growth was found at 420° in the presence of 100—150% excess of sodium hydroxide, yields of 100% then being recorded. As in the case of natural and synthetic albite, some differences in *X*-ray powder spacings were noted (Table 6) when compared with natural nepheline. Of moderate birefringence and straight extinction, the crystals had R.I. of $\varepsilon = 1{\cdot}537$, $\omega = 1{\cdot}534$, which are slightly lower than those of natural nepheline ($\varepsilon = 1{\cdot}542$, $\omega = 1{\cdot}538$, according to I.C.T., **1**, 153). The hexagonal unit-cell had dimensions $a = 4{\cdot}95$, $c = 8{\cdot}37$ Å.

Normal sodalite was found as spherulites up to 200 μ in diameter, but usually much smaller. The crystals were obtained in presence of excess of sodium chloride over the whole range of temperatures 150—450°, in yields up to 100%. They were isotropic with $n = 1{\cdot}488$, and belonged to the cubic system with unit-cell edge = 8·87 Å.

In addition, similar crystals of " basic " sodalite were grown at temperatures between 350° and 420° in the complete absence of sodium chloride but in the presence of a large excess (~300%) of the hydroxide. It was occasionally admixed with analcite, but was grown in 100% yields from analcite by treatment with aqueous sodium hydroxide at 400—450°. The cubic cell edges of these crystals varied between 8·77 and 8·90 Å, and although the intensities of the *X*-ray powder reflections were extremely similar to those of natural sodalite (Plate IX), yet small regular shifts in spacings occur. The R.I. of the more collapsed specimens was somewhat higher, with n reaching a limit of 1·495. Barth (*Z. Krist.*, 1932, **83**, 409) gave $a = 8{\cdot}89$ Å for natural sodalite.

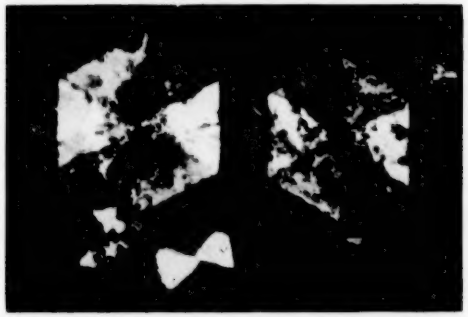
Normal and " basic " noseans (Plate VII) were formed under conditions of temperature and pH rather like those found effective for the sodalites. Normal nosean formed as spherulites up to 20 μ in diameter in presence of excess of sodium sulphate over the range 150—450°. The isotropic crystals had $n = 1{\cdot}486$ and a cubic cell edge of 9·10 Å. Basic nosean was grown as rhombic dodecahedra, often distorted, to a maximum dimension of 2 mm. 100% Yields were obtained at 450° in the presence of a great excess of sodium hydroxide (400—600%), and in the complete absence of the sulphate. It was also obtained in varying yields over a wide temperature and considerable pH range. *X*-Ray intensities were identical with those of natural nosean, but again shifts in the spacings occurred (Plate IX) corresponding to variations in the cubic cell edge between 9·03 and 9·10 Å. The isotropic crystals had R.I. which varied from 1·486 to 1·494. Mixtures of spherulites having nosean, sodalite, and analcite structures were grown from gels $Na_2O,Al_2O_3,1—3SiO_2$ at temperatures between 130° and 300°, in the presence of a small excess of sodium hydroxide (<100%). These compounds were usually of the collapsed type.

Normal cancrinite formed as thin rods, usually ~30 μ in length, when the gel $Na_2O,Al_2O_3,2SiO_2$ was treated with excess of aqueous sodium carbonate in the temperature interval 300—420°. Birefringence was moderate, with $\varepsilon = 1{\cdot}497$, $\omega = 1{\cdot}500$, and the system hexagonal, with unit cell dimensions of $a = 12{\cdot}63$, $c = 5{\cdot}18$ Å. " Basic " cancrinites (Plate VIII) were grown in complete absence of carbonate ion, but in the presence of excess of

PLATE I.

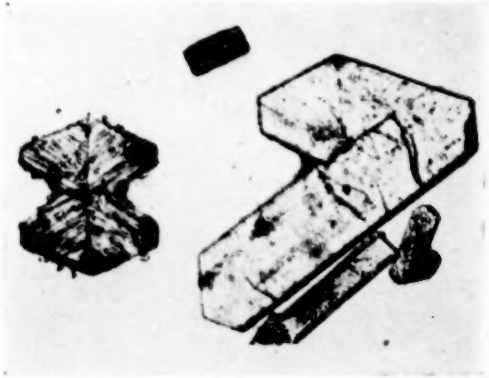
Analcite, showing three characteristic habits : spherulites (× 325); *cubes* (× 325); *and an ikositetrahedron* (× 522).

PLATE II.



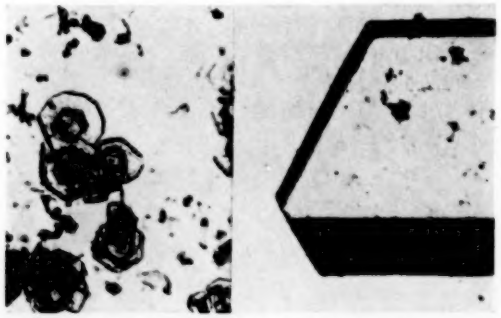
Left : *Nepheline hydrate I* (× 89). Right : *Nepheline hydrate II* (× 60). *Taken under crossed Nicols, and showing similarity in twinning.*

PLATE III.



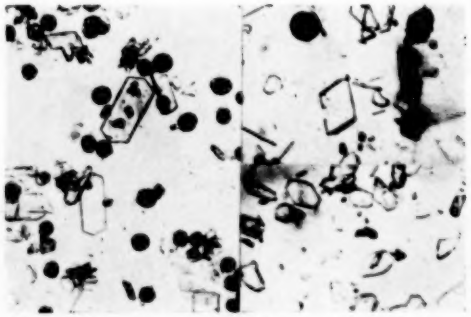
Nepheline hydrate I (left, × 125; right, × 100). *Characteristic crystals showing twinning. These crystals are of the* Ag^+ *ion-exchanged form; the striations shown, particularly on the left-hand crystal, are not visible in the* Na^+ *form.*

PLATE IV.



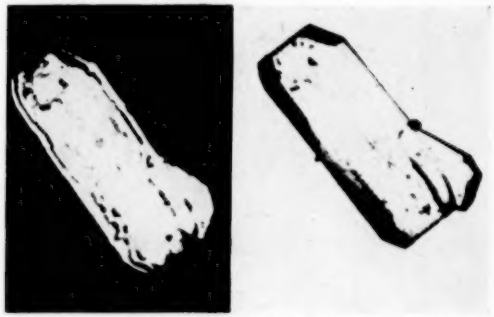
Left : *Plates of nepheline hydrate II overgrown on central hexagonal prism of nepheline* (× 120). Right : *Part of a crystal of compound* L (× 37·5).

PLATE V.



Characteristic forms of albite, together with some analcite spherulites. (Left, × 95; right, × 200.)

PLATE VI.



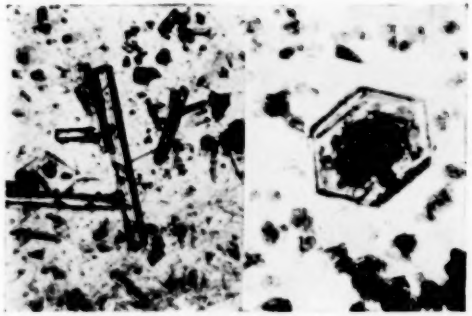
Nepheline crystal under crossed Nicols and in ordinary light. Internal irregularities in the crystal are clearly demonstrated in the left-hand photograph.

[*To face p.* 1566.

PLATE VII.

Left : *" Basic " nosean* (× 140). Right : *Compound* N (× 125).

PLATE VIII.



Left : *" Basic " cancrinite* (× 85). Right : *Compound* M (× 85). *The terraced structure is visible near the edges and causes the dark central portion.*

PLATE IX.

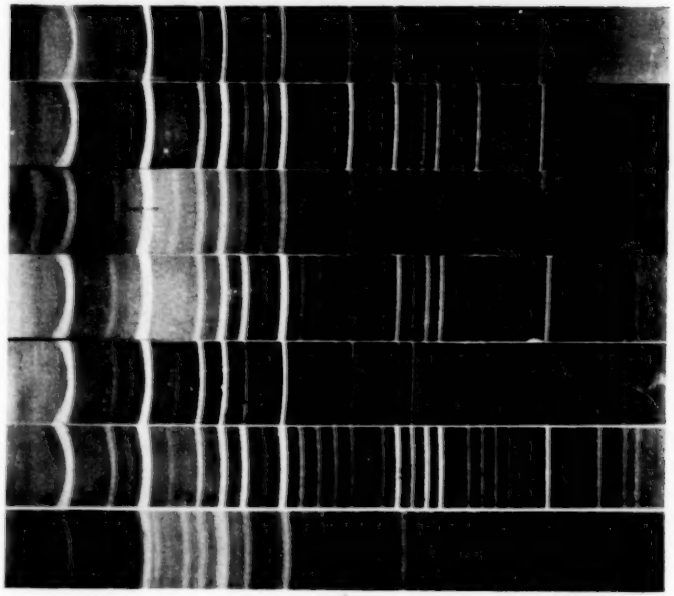
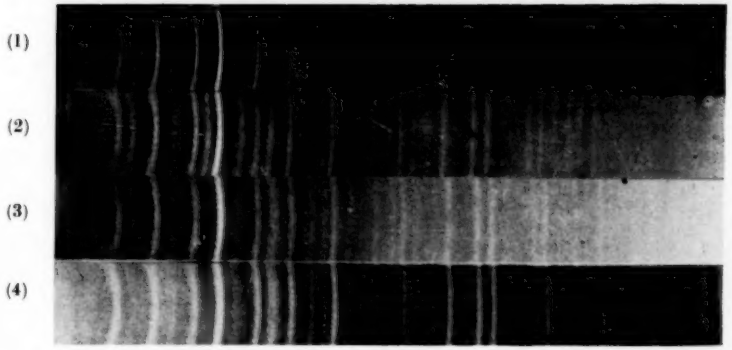


PLATE X.



Print of X-*ray powder photographs of different forms of " basic " cancrinite* (**1**, **3**, *and* **4**), *and of natural sulphatic cancrinite* (**2**).

PLATE IX.

Print of X-*ray powder photographs demonstrating the lattice changes in synthetic noseans and sodalites.*

(**1**) *and* (**2**) *Basic nosean.*
(**3**) *Nosean* (*with* SO_4^{--}).
(**4**) *and* (**5**) *" Basic " sodalites.*
(**6**) *Sodalite* (*with* Cl^-).
(**7**) *" Basic " Sodalite, with some analcite present.*

sodium hydroxide (200—300%), at ~390°. They occurred as small crystallites in masses and sometimes as hexagonal prisms up to 500 μ long. Although the *X*-ray powder photographs were almost identical with that of natural cancrinite, yet slight alterations in lattice spacing (Plate X) were found corresponding to expanded and contracted forms; variations in the unit-cell dimensions of these forms were $a = 12{\cdot}47$—$12{\cdot}71$ Å and $c = 5{\cdot}07$—$5{\cdot}20$ Å. Furthermore, the optical properties of different preparations showed a comparable variation (Table 4). The mean R.I. was ~1·50.

These remarkable " basic " noseans, sodalites, and cancrinites have not been observed in Nature. All three species are based upon a similar type of aluminosilicate framework (Bragg, " Atomic Structure of Minerals," Cornell Univ. Press, 1937), and it is noteworthy that these " basic " forms have been made by using the same gels ($n$$Na_2O$,$Al_2O_3$,$2SiO_2$,aq.) in all cases, and by varying only the amounts of excess of sodium hydroxide. As shown in Plate IX, compounds intermediate between a collapsed nosean and an expanded sodalite have been prepared, and it is likely that a continuous range of compounds is possible between the collapsed sodalite and expanded nosean structures, the formation of such a range being directly dependent upon the amount of sodium hydroxide present in the reacting mixture.

Other Products.—Two other crystal species were prepared in yields usually <50%. These are compounds M and N of Table 2. The former grew as hexagonal plates up to 250 μ across, and usually having a curious " terraced " structure (Plate VIII). Optimum yields were produced at 450° from the gel Na_2O,Al_2O_3,$2SiO_2$, with excess of sodium hydroxide present (>100%). The crystals were often a secondary phase in nosean preparations and could be separated by hand-picking. Belonging to the orthorhombic system, the crystals had a mean R.I. ~1·635, and unit-cell dimensions of $a = 11{\cdot}75$, $b = 5{\cdot}81$, $c = 8{\cdot}52$ Å.

Compound N was produced as very thin needles in bunches, single crystals often having a length : thickness ratio of ~300 : 1 (Plate VII). They grew in varying yields as a secondary phase, from gels Na_2O,Al_2O_3,6—$8SiO_2$ at ~360° in the presence of a moderate excess of sodium hydroxide (~100%). Refractive indices were $\varepsilon = 1{\cdot}616$ and $\omega = 1{\cdot}612$, the probable system being hexagonal. On treatment with aqueous silver nitrate at 110°, ion-exchange occurred and the product had a mean R.I. > 1·77. Attempts at separation of these crystals were unsucessful and *X*-ray data were not obtainable.

Large acicular crystals, almost 1 cm. long, were found attached to the autoclave stoppers after some experiments with gels of high silica content and a large excess of sodium hydroxide (>300%) at temperatures of ~390°. On *X*-ray examination these proved to be of anhydrous Na_2SiO_3.

Exchange Reactions with Dry Hydrogen Chloride.—The basic noseans, sodalites, and cancrinites could contain only H_2O or NaOH in place of the usual intercalated Na_2SO_4, NaCl, or Na_2CO_3. Little water was liberated by outgassing at 300—350°, however, so the interstitial compound was thought to be sodium hydroxide. To test this, the crystals were thoroughly outgassed and then exposed to dry hydrogen chloride at temperatures >100°. A steady irreversible sorption was observed, the more rapid the higher the temperature. If the temperature was high enough, water was simultaneously liberated and condensed on the walls of the apparatus. The amounts of hydrogen chloride sorbed are shown in Table 3. Thus a reaction such as

$$HCl(gas) + NaOH(intracrystalline) \longrightarrow H_2O(intracrystalline) + NaCl(extracrystalline)$$

had occurred, and must involve migration of H^+ into the crystals and equivalent migration of Na^+ out of the crystals. The presence of solid sodium chloride was revealed by *X*-ray powder photographs of the hydrogen chloride-treated material. The original reflection intensities of the aluminosilicates were weakened and there was also increased background scattering, suggesting some breakdown during the exchange, probably associated with a second type of reaction (with hydrogen chloride) described below.

The $Na^+ \rightleftharpoons H^+$ exchange diffusion recalls the behaviour of the glass electrode; the use of dry hydrogen chloride, however, is an extension of Clarke and Steiger's method of effecting ion exchange by using gaseous ammonium chloride (*Amer. J. Sci.*, 1902, **13**, 27; *Z. anorg. Chem.*, 1902, **29**, 338). Like NH_4^+, H^+ readily migrates into the lattice but the larger Cl^- ion remains outside the crystal.

Barth (*loc. cit.*) assigns to sodalite and nosean structures in which *all* Na^+ ions occupy nearly equivalent positions in the lattice. Thus the sodium hydroxide is present as Na^+ and OH^- ions, and, moreover, there seems no reason why exchange of Na^+ for H^+ should be limited to a number

of such ions equal to the number of OH^- ions present; rather, *all* the Na^+ ions should be able to exchange, but with possible different results (see below). To investigate exchange of other Na^+ ions, crystals of analcite and particles of a silicate glass containing 16% of sodium oxide were exposed to dry hydrogen chloride. Both reacted to a considerable extent (Table 3), and *X*-ray examination showed solid sodium chloride to be formed in each case. The reaction here must be represented as

$$\geqslant Si{-}O^- \ldots Na^+ + HCl\ (gas) \longrightarrow \geqslant Si{-}OH + NaCl\ (extracrystalline)$$

On heating to ~250° some water was liberated, so that further reaction occurs:

$$\geqslant Si{-}OH + HO{-}Si\leqslant \longrightarrow \geqslant Si{-}O{-}Si\leqslant + H_2O$$

This reaction forms a collapsed silica glass coating round the particles, and may be expected to prevent or retard exchange diffusion, as well as to account for the *X*-ray evidence of partial decomposition of the H^+-ion exchanged sodalite, nosean, and cancrinite (see above).

TABLE 3. *Exchange sorption of dry* HCl *by several crystals.*

Mineral	HCl sorbed (c.c. at N.T.P./g.)	Max. temp. reached	% Total Na^+ ions exchanged in mineral	Refractive indices Before exchange	Refractive indices After exchange
Analcite	28·5	360°	~28	1·487	1·455
Cancrinite (formed in absence of CO_3^{--})	125	250	66·3	1·50 (mean)	1·460
Nosean (formed in absence of SO_4^{--})	50·1	250	26·5	1·494	1·365
Nosean (formed in presence of SO_4^{--})	30·8	250	17·1	1·486	~1·46
Sodalite (formed in absence of Cl^-)	99·1	250	52·5	1·488	~1·47
Silicate glass	25·7	200	18·2	—	—

Dehydrated chabazite also gave some reaction with dry hydrogen chloride, although in this case, before reaction, *molecular* hydrogen chloride was absorbed and sodium and calcium chlorides were produced interstitially, and could be extracted hydrothermally (Barrer and Brook, in preparation). One may conclude that a substantial degree of exchange of Na^+ by H^+ can occur in a variety of minerals. It is most marked for the " basic " cancrinites, sodalites, and noseans of the previous section, probably because these contain reactive sodium hydroxide intercalated in place of the usual salts.

Optical and Other Properties of " Basic " Cancrinites.—A number of preparations of cancrinites were carried out from gels $Na_2O,Al_2O_3,2SiO_2$ but with variable amounts of sodium hydroxide and carbonate in the mother-liquors. These cancrinites were investigated by *X*-rays and optically, with the results shown in Table 4.

TABLE 4. *Some properties of synthetic cancrinite.*

Growth medium	Refractive indices ε	Refractive indices ω	Elongation	Lattice type compared with a natural cancrinite
NaOH aq.	1·504	1·501	+	Slightly expanded
Na_2CO_3 + NaOH aq.	1·498	1·502	—	Considerably collapsed
NaOH aq.	1·497	1·500	—	Identical
NaOH aq.	1·498	1·494	+	Slightly collapsed
NaOH aq.	1·504	1·498	+	Slightly collapsed
Na_2CO_3 aq.	1·498	1·501	—	Slightly collapsed

TABLE 5. *Ignition products.*

Species	Ignition loss, %	Product	Species	Ignition loss, %	Product
Albite	Negligible	Albite	Basic sodalite	3·3	Carnegieite
Analcite	8·3	Albite	Mordenite	13·5	Glass
Normal cancrinite	7·9	Glass	Nepheline	Negligible	Nepheline
Basic cancrinite	5·9	Nepheline	Paragonite	4·3	Mullite
Normal nosean	10·8	Nepheline	Compound L	7	Glass
Basic nosean	14·2	Carnegieite	Nepheline hydrate I	9·6	Nepheline
Normal sodalite	7·4	Nepheline	Nepheline hydrate II	2·0	Nepheline

TABLE 6. *X-Ray data for typical species (spacings in Å).*

Synthetic albite		Natural albite		Synthetic nepheline		Natural nepheline		Nepheline hydrate I	
I	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*
w	6·49	w	6·40	mw	4·68	—	—	ms	8·3
w	4·27	vw	4·33	w	4·30	—	—	ms	7·4
mw	4·03	ms	4·05	ms	4·16	s	4·18	mw	$6\cdot3_8$
mw	3·76	m	3·78	s	3·83	vw	3·83	m	$5\cdot5_2$
w	3·63	m	3·69	mw	3·66	—	—	vw	$4\cdot7_2$
ms	3·35	mw	3·36	vs	3·26	s	3·27	vs	4·39
vs	3·18	vs	3·19	—	—	w	3·17	vw	4·11
mw	2·92	ms	2·94	vs	3·00	vvs	3·00	vw	3·61
vw	2·83	vvw	2·84	w	2·88	s	2·88	vvs	3·40
vvw	2·75	vvw	2·74	w	2·73	—	—	vw	3·22
vw	2·64	vw	2·65	mw	2·57	m	2·57	vs	2·95
mw	2·50	w	2·55	mw	2·49	mw	2·49	ms	2·84
vvw	2·45	vvw	2·44	mw	2·41	w	2·39	s	2·60
mw	2·28	vw	2·32	w	2·34	ms	2·34	s	2·43
vvw	2·21	vw	2·19	mw	2·30	mw	2·30	vw	2·30
w	2·12	vw	2·12	w	2·13	vw	2·12	mw	2·19
w	2·09	vw	2·07	w	2·09	mw	2·08	w	2·11
vw	1·87	w	1·89	mw	1·98	vvw	1·98	vw	2·05
mw	1·82	w	1·83	w	1·93	m	1·93	vw	1·97
w	1·78	vw	1·78	vvw	1·88	mw	1·88	m	1·86
vw	1·606	vw	1·603	vw	1·85	vw	1·84	vw	1·84
vw	1·571	vvw	1·561	vw	1·79	mw	1·79	w	1·80
—	—	vw	1·509	vw	1·75	vvw	1·76	vw	1·74
—	—	vw	1·465	w	1·70	w	1·70	w	1·70
				—	—	mw	1·62	vw	1·61
				w	1·59	w	1·60	vw	1·58
				m	1·56	ms	1·56	w	1·57
				—	—	w	1·52	vw	1·52
				vw	1·46	vw	1·46		

Nepheline hydrate II		Synthetic paragonite		Natural paragonite •		Species L		Species M	
I	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*
mw	6·27	m	9·5	60	9·3	s	5·97	vvs	9·7
vw	5·49	—	—	40	4·97	m	4·30	vw	5·94
s	4·67	vw	4·77	30	4·72	ms	3·96	w	4·10
ms	4·34	ms	4·39	100	4·39	w	3·77	w	3·96
vs	4·07	w	4·21	—	—	ms	3·62	ms	3·56
w	3·84	vw	4·01	60	4·01	w	3·21	mw	3·46
s	3·67	—	—	70	3·74	m	3·06	w	3·33
ms	3·40	—	—	60	3·65	s	2·97	ms	3·19
s	3·24	w	3·50	—	—	mw	2·67	w	2·97
w	3·16	—	—	50	3·27	m	2·58	mw	2·84
vvs	2·95	s	3·18	70	3·14	ms	2·43	mw	2·73
mw	2·84	mw	3·03	40	2·93	w	2·34	mw	2·65
mw	2·74	—	—	60	2·87	w	2·27	ms	2·42
m	2·59	vw	2·79	50	2·77	w	2·14	vw	2·37
mw	2·49	vs	2·51	100	2·52	w	2·07	vw	2·31
w	2·44	m	2·41	70	2·41	mw	1·89	w	2·27
w	2·30	w	2·34	60	2·33	ms	1·82	vw	2·21
w	2·27	w	2·17	60	2·16	vw	1·78	ms	2·07
w	2·20	m	2·08	70	2·09	w	1·75	w	1·97
mw	2·13	mw	1·92	60	1·90	vw	1·70	w	1·90
vw	2·08	vvw	1·82	40	1·83	vw	1·67	vw	1·79
mw	2·04	w	1·67	60	1·67	mw	1·61	m	1·61
vw	1·97	mw	1·60	60	1·60	w	1·58	w	1·56
w	1·91	vvw	1·55	40	1·57	vw	1·55	m	1·51
vw	1·88	vvs	1·48	100	1·47			w	1·48
vw	1·84	vvw	1·37	20	1·37			mw	1·42
w	1·76	vw	1·34	50	1·34			mw	1·40
vw	1·70	vw	1·31	50	1·30			mw	1·38
		vw	1·28	60	1·28			m	1·35
		vvw	1·25	50	1·25				
		vw	1·23	60	1·23				

• " Alphabetical Index of *X*-Ray Data " (American Soc. Testing Materials).

The optical character is seen to be variable and could not apparently be correlated with any one factor. Ion exchange of Ag^+ for Na^+ also gave products, differing optically *inter se*, when made from the above variable forms of cancrinite. Of two specimens treated under identical conditions with saturated silver nitrate solution at 110°, one gave a crystalline product almost isotropic and with R.I. = 1·647, while the other yielded crystals with very high birefringence, having $\varepsilon \sim 1{\cdot}640$ and $\omega \sim 1{\cdot}670$. The *X*-ray powder photographs of both showed them to be ion-exchanged cancrinites with, however, some intensity differences between them.

Wyart (*loc. cit.*) has recorded a cancrinitic phase which had a composition approximating to $Na_2O,Al_2O_3,2SiO_2,2H_2O$, together with a small amount of sodium carbonate. This cancrinite gave $\varepsilon = 1{\cdot}489$ and $\omega = 1{\cdot}492$, and may be in part analogous to the preparations here described. Our "basic" cancrinites are, moreover, rather similar in *X*-ray spacings to the "phase X" grown by Friedman (*loc. cit.*), for which the analysis corresponds to $13Na_2O,9Al_2O_3,22SiO_2,H_2O$. One has thus further reason to formulate these basic cancrinites as $3(Na_2O,Al_2O_3,2SiO_2),xNaOH,yH_2O$, where x and y may be variable and possibly interrelated. One might by analogy with natural cancrinites assume than when $x = 2$, $y = 0$, and, considering Wyart's cancrinitic phase, that if $x = 0$, $y = 2$.

The reason for the occurrence of these variable basic cancrinites or, under somewhat different conditions, basic noseans and sodalites, remains, however, obscure. It may be that, by changing the pH, the proportions of sodium hydroxide and of water which are intercalated are modified progressively, and that these changes are accompanied at certain stages by modifications in the aluminosilicate framework.

Ignition Products.—The crystalline products were ignited in a platinum crucible over a Meker burner at ~1150° (measured by Pt/Pt–Rh thermocouple). Ignition losses and products identified by *X*-ray powder photography are given in Table 5. The formation of carnegieite can be ascribed to slightly increased ignition temperature; the nepheline–carnegieite inversion occurs at ~1250° for compositions $Na_2O,Al_2O_3,2SiO_2$. Minerals obtained on ignition are well-known refractory materials.

Ion-exchange Reactions.—The relatively open framework structures of cancrinite, sodalite, and nosean should enable them to show cation exchange similar to that in zeolites. Saturated silver nitrate solution at 110° was found after 2 days to effect exchange with each mineral, as demonstrated by changes in refractive indices and *X*-ray powder diffraction patterns and by analysis. Similar attempts to introduce Ag^+ ions into albite, nepheline, and paragonite were on the other hand unsuccessful, although Silber (*Ber.*, 1881, **14**, 941) has claimed that one-third of the Na^+ in nepheline can be exchanged by Ag^+ under similar conditions.

Crystals of nepheline hydrate I were found to exchange Na^+ readily for Tl^+ or Ag^+ under mild hydrothermal conditions, whereas nepheline hydrate II was in this respect inert. This suggests that nepheline hydrate I has the more open frame-work structure, and is compatible with its lower refractive indices.

Discussion

Analcite occurs over a very wide range of temperature and composition, at moderate pH (~9). Friedman (*loc. cit.*) nevertheless considers that analcite is a metastable phase and that even at 400° true equilibrium is not established in less than about 10 days in contact with the mother-liquor. However, except at the higher temperatures this view is not supported in the present work. Recrystallisation of analcite was not observed when these crystals were kept for abnormal periods in contact with the crystallisation media. Although many metamorphoses of this zeolite were possible, special conditions were usually required for such transformations (Barrer, Hinds, and White, in preparation). Moreover, by using gels as starting materials for hydrothermal crystallisation rather than homogenised glasses, crystal growth is more rapid, and can be studied to much lower temperatures, so that equilibrium conditions may be more quickly approached.

However, the preparation of the most stable phases only was not the full objective of the present research: often the most interesting properties are associated with metastable crystals; mordenite, for example, when grown in media of high pH soon disproportionates to give other phases such as analcite (Barrer, *loc. cit.*). Nevertheless, it may be reproducibly formed.

A feature of the aluminosilicate chemistry both of lithium (Part I, *loc. cit.*) and of sodium (this paper) has been the preparation of species without natural counterparts, or

which are variants of naturally occurring minerals. Moreover, the basic cancrinites, noseans, and sodalites reported here, with stoicheiometric and physical differences from their natural counterparts, by no means complete the limits of adaptability possessed by this type of aluminosilicate framework. Sodalite-type crystals have also been prepared where the intercalated salts are sodium bromide and nitrate (Flint, Clarke, Newman, Shartis, Bishop, and Wells, *J. Res. Nat. Bur. Stand.*, 1945, **36**, 63). With only minor structural changes it would appear that replacements are possible in the sodalite-nosean framework covering at least NaCl, NaBr, NaOH, Na_2CO_3, $NaNO_3$, and H_2O, while with cancrinite the replacements Na_2SO_4, Na_2CO_3, NaOH, and H_2O are found. Such exchanges are not effected directly, but by hydrothermal synthesis of the various forms.

One may note that this kind of replacement (through direct synthesis, not by ion-exchange) is observed among other aluminosilicate minerals. It is well shown among the felspars ($K \rightleftharpoons Na \rightleftharpoons Ca \rightleftharpoons Ba$; also $Al \rightleftharpoons Ga$ and $Si \rightleftharpoons Ge$) (Goldsmith, *J. Geol.*, 1950, **58**, 518), while with synthetic mica an extraordinary degree of diadochic replacement has been discovered (Hatch, Eitel, and Humphrey, U.S. Naval Res. Report on Synthetic Micas, 1949). Similarly, by direct synthesis, a number of diadochic forms have been prepared based on the analcite structure (Barrer and McCallum, in preparation). In each such series of crystals the permanent aluminosilicate frameworks show considerable powers of adjustment, but always as variants of a pattern characteristic of the series.

Although some of the species grown under these alkaline conditions were not of robust three-dimensional network type (*e.g.*, paragonite at lower pH), by far the greater proportion of the crystals were of this kind. It seems that alkaline mother-liquors and 1 : 1 ratio between Na_2O and Al_2O_3 in the gel lead preferentially to framework aluminosilicates. A problem unsolved by this study concerns the conditions of growth for the fibrous aluminosilicates, such as natrolite ($Na_2O,Al_2O_3,3SiO_2,2H_2O$). Despite claims in the earlier literature (Thugutt, *Neues Jahrb. Min.*, Beil. Bd., 1894, **9**, 554; Friedel and Grandjean, *Bull. Soc. Min.*, 1909, **32**, 150; Gruner, *Z. anorg. Chem.*, 1929, **182**, 319), no natrolite was observed among the numerous species formed in the present work. It is possible that at least some of the earlier claims may have referred to cancrinite, which grows as acicular crystals comparable with natrolite in form and refractive index (for natrolite, $n \sim 1{\cdot}49$; for cancrinite, $n \sim 1{\cdot}50$).

Although the compounds described here were grown only in small amounts, there seems no reason why many of them could not be obtained in quantity. The average size of individual crystals in the sodium aluminosilicate field usually exceeded that of the lithium aluminosilicate crystals (Part I, *loc. cit.*). In a single preparation, and without growing on seeds, crystals of 1—5 mm. were sometimes obtained. If the pH of the mother-liquor is properly adjusted, it is possible, by using a seed crystal and, as feed material, small synthetic crystals of the same species grown as described in this paper, that still larger crystals could be made. The method of deposition on the seed by using a moderate thermal gradient and placing the seed in the colder part of the alkaline mother-liquor, has for example proved successful in growing large quartz crystals (Brown, Kell, Thomas, Wooster, and Wooster, *Nature*, 1951, **167**, 940), and is probably of some general applicability.

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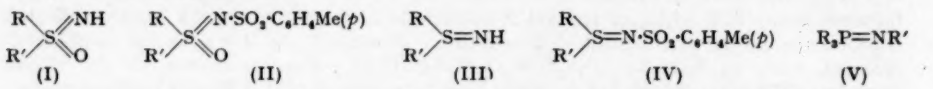
287. *Preparation and Properties of Some Aliphatic Sulphoximines.*

By J. K. Whitehead and H. R. Bentley.

A number of aliphatic sulphoximines have been synthesised by the alternative routes of the action of hydrazoic acid on the appropriate sulphides or sulphoxides in the presence of concentrated sulphuric acid and by the hydrolysis of toluene-*p*-sulphonylsulphoximides. It has been shown that the former reaction is of general application whereas the success of the latter method depends upon the state of substitution of the alkyl groups in the starting material.

Some reactions of sulphoximines are examined.

Dimethylsulphoximine (I; R = R′ = Me) was first synthesised by the hydrolysis of toluene-*p*-sulphonyldimethylsulphoximide (II; R = R′ = Me) by means of concentrated sulphuric acid (Bentley and Whitehead, *J.*, 1950, 2081). Bentley, McDermott, and Whitehead (*Nature*, **1950**, **165**, 735; *Proc. Roy. Soc.*, **1951**, *B*, **138**, 265) later synthesised dimethylsulphoximine by the action of hydrazoic acid on dimethyl sulphoxide. dl-Methionine and *S*-methyl-l-cysteine sulphoxides were also converted into the corresponding sulphoximines by the second route. These synthetic methods have now been extended in relation to certain aliphatic sulphoximines and some reactions of the latter have been examined.



(I) (II) (III) (IV) (V)

The nomenclature of these compounds is now presented on a logical basis. The name "sulphoximine" was earlier adopted (*J.*, 1950, 2081) for the series typified by (I), as an acceptable contraction of "sulphoxidimine" which follows logically by comparison with the phosphinimines (V). The naming of (II) as toluene-*p*-sulphonyldialkylsulphoximides then follows. Substance of type (III), of which the parent is unknown, have hitherto been called "dialkylsulphilimines" but are now named "dialkylsulphidimines" again by analogy with "phosphinimine"; compounds of type (IV), typical of the stable series of toluenesulphonated sulphilimines, then become "toluene-*p*-sulphonyldialkylsulphidimides" and not "dialkylsulphintoluene-*p*-sulphonylimines."

The preparation of sulphoximines by the isolation of the corresponding toluene-*p*-sulphonylsulphoxidimines, followed by hydrolysis of the toluene-*p*-sulphonylsulphoximides produced, is not a general reaction. On the other hand, the alternative synthesis by the action of hydrazoic acid on the corresponding sulphoxides appears to be of general application.

The S–N linkage in simple aliphatic sulphidimides is easily severed by dilute acids (Holloway, Kenyon, and Phillips, *J.*, 1928, 3000). Substitution in the alkyl groups appears to weaken this linkage still further. Previous results indicate that sulphidimines cannot be formed from heavily substituted sulphides. For instance, Mann and Pope (*J.*, 1922, **121**, 1052) were unable to prepare sulphidimides from derivatives of diethyl sulphide containing more than two chlorine atoms, and Tarbell and Weaver (*J. Amer. Chem. Soc.*, 1941, **63**, 2939) were unable to condense bis-2-hydroxyethyl sulphoxide with toluene-*p*-sulphonamide although a hydrated sulphidimide does result from the action of chloramine-t on the corresponding sulphide. Further, neither methionine nor its sulphoxide gives a sulphidimide when treated with chloramine-t and with toluene-*p*-sulphonamide respectively (Bentley, McDermott, and Whitehead, *loc. cit.*, 1951). We have now prepared the sulphidimides (IV; R = Me, R′ = CH_2·CH_2Cl or CH_2·CH_2·OH) from 2-chloroethyl and 2-hydroxyethyl methyl sulphide, respectively.

The stability of the S=N bond in sulphidimides under oxidising conditions is the limiting factor in attempts to extend the synthesis of sulphoximides by oxidation of the former with permanganate. Oxidation of (IV; R = Me, R′ = CH_2·CH_2Cl or CH_2·CH_2·OH) with

potassium permanganate in water, aqueous sodium hydroxide, or acetic acid gave toluene-*p*-sulphonamide in each case; with potassium permanganate or perhydrol in acetone, the appropriate sulphidimide is recovered unchanged. The alternative synthesis of sulphoximides by use of hydrazoic acid involves the formation of a nitrogen bond to a sulphur atom already carrying an oxygen atom. This appears to be a general reaction throughout the range of compounds studied. Diethyl-, methyl-*n*-propyl-, and *n*-butylmethyl-sulphoximines are formed from the appropriate sulphoxides by this method, and Misani, Fair, and Reiner (*J. Amer. Chem. Soc.*, 1951, **73**, 459) have prepared diamylsulphoximine and several aromatic sulphoximines by the same route.

The increased stability of the S–N bond on a sulphur atom also carrying an oxygen atom is further illustrated by the extreme resistance of the sulphoximines to hydrolysis by acid. The bond, however, is readily broken by oxidising agents, as in the oxidation of methioninesulphoximine to methionine sulphone by perhydrol (Misani and Reiner, *Arch. Biochem.*, 1950, **27**, 234). It is also broken by nitrous acid, and dimethylsulphoximine is readily converted into dimethyl sulphone by this reagent.

Sulphoximines can also be prepared by the action of hydrazoic acid directly on the corresponding sulphide; *e.g.*, dimethyl sulphide with 2 mols. of hydrazoic acid in chloroform and concentrated sulphuric acid gives a product from which both dimethyl sulphoxide and dimethylsulphoximine can be recovered; under the same conditions also, methionine is converted directly into its sulphoximine. A sulphide and hydrazoic acid probably give first the unstable sulphidimine (III), but we could not isolate such a derivative which must therefore be hydrolysed at once to the sulphoxide which then reacts normally with a further molecule of hydrazoic acid.

Sulphoximines are more basic than the corresponding sulphoxides but otherwise resemble them closely in physical properties. In the final mixture produced in the hydrazoic acid synthesis partition between the two layers is greater in the acid layer for the sulphoximine and in the chloroform layer for untreated sulphoxide. Partition is, however, by no means complete in either case. The only crystalline salts of sulphoximines which we have obtained are picrates which are useful for characterisation.

Dimethylsulphoximine and sodium in an inert solvent form the unstable hygroscopic *N*-sodio-derivative, the structure of which follows from its ready reaction with toluene-*p*-sulphonyl chloride to give toluene-*p*-sulphonyldimethylsulphoximide.

Experimental

Diethylsulphoximine.—Under conditions described by Bentley, McDermott, and Whitehead (*loc. cit.*, 1951), diethyl sulphoxide (7·7 g.), sodium azide (5·6 g.), and sulphuric acid (*d* 1·84; 25 ml.) in chloroform (100 ml.) gave *diethylsulphoximine* (3·3 g., 49%) as a colourless oil, b. p. 135—140° (bath-temp.)/0·1 mm. (Found: C, 39·5; H, 9·4. $C_4H_{11}ONS$ requires C, 39·4; H, 9·1%); the *picrate* had m. p. 122—123° (Found: C, 34·6; H, 4·3; N, 16·0. $C_4H_{11}ONS,C_6H_3O_7N_3$ requires C, 34·3; H, 4·3; N, 16·0%).

*Methyl-*n*-propylsulphoximine.*—Similarly, methyl *n*-propyl sulphoxide (5·0 g.), sodium azide (3·1 g., 1·2 mols.), and sulphuric acid (*d* 1·84; 15 ml.) in chloroform (75 ml.) give *methyl-*n*-propylsulphoximine* (2·3 g., 13%), b. p. 180—185° (bath-temp.)/0·1 mm. (Found: C, 39·2; H, 9·2. $C_4H_{11}ONS$ requires C, 39·4; H, 9·1%) [*picrate*, m. p. 112° (Found: C, 34·2; H, 4·0; N, 15·9. $C_4H_{11}ONS,C_6H_3O_7N_3$ requires C, 34·3; H, 4·3; N, 16·0%)].

n-*Butylmethylsulphoximine.*—Similarly, *n*-butyl methyl sulphoxide (30·0 g.), sodium azide (19·5 g., 1·2 mols.), and sulphuric acid (*d* 1·84; 90 ml.) in chloroform (450 ml.) gave this sulphoximine as an oil which could not be distilled without decomposition; its *picrate* had m. p. 118° (Found: C, 36·5; H, 4·6; N, 15·5. $C_5H_{13}ONS,C_6H_3O_7N_3$ requires C, 36·2; H, 4·7; N, 15·4%).

*Toluene-*p*-sulphonyl-2-chloroethylmethylsulphidimide.*—2-Chloroethyl methyl sulphide (11·0 g.) was shaken with a solution of chloramine-T (23·0 g., 1 mol.) in water (200 ml.) until precipitation was complete. The product (23·0 g., 82%) was collected, washed with water, and recrystallised from ethanol, giving the *sulphidimide* as small needles, m. p. 124° (Found: C, 43·1; H, 5·1; N, 5·15. $C_{10}H_{14}O_2NClS_2$ requires C, 42·9; H, 5·0; N, 5·0%).

*Toluene-*p*-sulphonyl-2-hydroxyethylmethylsulphidimide.*—2-Hydroxyethyl methyl sulphide (9·2 g.) and chloramine-T (23·0 g., 1 mol.) were dissolved in the minimum of hot ethanol; the

solution was kept for 30 minutes, filtered from sodium chloride, and concentrated. The solid product was collected and recrystallised from benzene, giving the *sulphidimide* (16·0 g., 61%) as clusters of rods, m. p. 108° (Found: C, 45·8; H, 5·7; N, 5·15. $C_{16}H_{18}O_3NS_2$ requires C, 46·0; H, 5·75; N, 5·4%).

Attempted Oxidations.—Oxidation of these derivatives with potassium permanganate (1 or 2 mols.) in water, aqueous sodium hydroxide, or acetic acid gave toluene-*p*-sulphonamide. The sulphidimides were recovered unchanged after treatment with potassium permanganate (5 mols.) or perhydrol (1 mol.) in boiling acetone.

Dimethylsulphoximine.—Sodium azide (40·0 g., 2 mols.) was added in small portions during 6 hours to a vigorously stirred mixture of dimethyl sulphide (20·0 g.), sulphuric acid (*d* 1·84; 75 ml.), and chloroform (200 ml.) kept at 40° in a flask fitted with a reflux condenser. The product finally recovered from the aqueous acid layer (Bentley, McDermott, and Whitehead, *loc. cit.*) was distilled, giving dimethyl sulphoxide (2·0 g.), b. p. 92—95°/20 mm. (Found: C, 31·3; H, 8·0. Calc. for C_2H_6OS: C, 30·8; H, 7·7%), and dimethylsulphoximine (3·3 g.), b. p. 155—160°/20 mm. (picrate, m. p. 179° alone or mixed with an authentic specimen).

Methionine Sulphoximine.—Under similar conditions DL-methionine (5·0 g.), sodium azide (4·7 g., 2·4 mols.), and sulphuric acid (*d* 1·84; 30 ml.) in chloroform (100 ml.) gave DL-methionine sulphoximine (1·8 g., 27%), m. p. 219° alone or mixed with an authentic sample, identical with an authentic specimen on paper chromatograms (phenol and acetone).

N-*Sodio-dimethylsulphoximine.*—A solution of dimethylsulphoximine (0·25 g.) in dry benzene (25 ml.) was boiled under reflux with finely divided sodium (0·10 g.) until reaction had ceased. Unchanged sodium was removed mechanically from the suspension of yellow sodio-derivative, and toluene-*p*-sulphonyl chloride (0·3 g.) was then added to the mixture. After 30 minutes' refluxing, during which time sodium chloride slowly separated, the mixture was evaporated to dryness, hot water (10 ml.) was added to the residue, and the hot solution filtered; the cooled filtrate finally deposited needles, m. p. 167—169° alone or mixed with an authentic specimen of toluene-*p*-sulphonyldimethylsulphoximide.

Deamination of Dimethylsulphoximine.—Solutions of sodium nitrite (1·6 g.) in water (50 ml.) and of hydrochloric acid (*d* 1·18; 2·5 ml.) in water (50 ml.) were added together dropwise with stirring to a solution of dimethylsulphoximine (2·0 g.) in water (50 ml.) and hydrochloric acid (*d* 1·18; 2·5 ml.) at 75—80°. The final solution was evaporated to dryness under reduced pressure, the residue was redissolved in water (10 ml.), again evaporated, and then dissolved in water (20 ml.), and the solution extracted with ether (2 × 20 ml.). Unchanged dimethylsulphoximine (picrate, m. p. 179° alone or with an authentic specimen) was recovered from the ethereal extract. The aqueous fraction was evaporated to dryness under reduced pressure, the dry residue was extracted with acetone, and the acetone-soluble product was distilled, giving dimethyl sulphone, b. p. 170—180°/20 mm., m. p. 103—104° (Found: C, 26·0; H, 6·7. Calc. for $C_2H_6O_2S$: C, 25·5; H, 6·4%).

RESEARCH ASSOCIATION OF BRITISH FLOUR MILLERS, CEREALS RESEARCH STATION, OLD LONDON ROAD, ST. ALBANS, HERTS.
ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, December 21st*, 1951.]

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288. *Amino-acids and Peptides. Part VIII.* Determination of* D- *and* L-*Glutamic Acid by the Isotope-dilution Method.*

By C. C. BARKER, I. W. HUGHES, and G. T. YOUNG.

A new method based on the isotope dilution principle has been developed for the determination of the total (D- + L-)glutamic acid in mixtures of amino-acids. In control experiments with synthetic mixtures the glutamic acid found was 99·2—99·3% of the theoretical amount. The procedure has been applied to the analysis of gliadin.

ACCURATE determination of both enantiomorphs of an amino-acid in a protein hydrolysate is difficult. Procedures based on partition chromatography (*e.g.*, Moore and Stein, *Ann. N.Y. Acad. Sci.*, 1948, **49**, 265) and on ion-exchange (*e.g.*, *idem*, *J. Biol. Chem.*, 1951, **192**, 663) determine the total of both isomers (D and L), but so far their accuracy appears to be

* Part VII, *J.*, 1952, 594.

rather less than is often desirable for investigations of protein structure. The isotope-dilution principle, avoiding as it does the difficulty of quantitative isolation, is clearly attractive for this purpose. In its most usual application, the L-amino-acid is isolated and therefore this form only is assayed. A modification has already been used by which both enantiomorphs of glutamic acid have been determined (Graff, Rittenberg, and Foster, *J. Biol. Chem.*, 1940, **133**, 745; Wieland and Paul, *Ber.*, 1944, **77**, 34). Isotopic DL-glutamic acid hydrochloride is added to the mixture to be analysed, from which pure L- and DL-glutamic acid hydrochlorides are then isolated; from the isotopic dilution of these two samples, the amount of D(and L)-glutamic acid may be calculated. It is however sometimes difficult to isolate the pure racemate, since it is normally present in low concentration and has a higher solubility than the enantiomorphs, and it is then necessary to determine the composition of the mixture of isomers by measuring its optical rotation.

We have developed an alternative method for the determination of the total (D- and L-)glutamic acid, using the isotope-dilution principle. A known weight of L-[^{15}N]glutamic acid hydrochloride is added to the amino-acid mixture, which is then benzoylated, and the solution is treated with acetic anhydride at room temperature for 48 hours. Under these conditions, benzoylglutamic acid is racemised and after hydrolysis of the benzoyl derivatives a sample of DL-glutamic acid hydrochloride can readily be isolated in the normal way. From the isotopic dilution, the total glutamic acid originally present can be calculated directly. Loss of glutamic acid before racemisation is achieved will affect the determination only if optical isomers are lost differentially, whilst after racemisation such loss will cause no error. Control experiments showed that under the above conditions benzoyl-L-glutamic acid is racemised to the extent of 97·5%; calculation shows that no appreciable error is introduced by this incompletion. For example, if 5% of the glutamic acid is originally present as the D-form and if racemisation is 95% complete, the error is less than 0·03% of the total glutamic acid (if isotopic dilution is 1 : 10).

This procedure has been tested by the analysis of known mixtures of amino-acids, containing both D- and L-glutamic acid. The isolation and conversion of the samples into nitrogen, and the mass-spectrometric analyses (for which we are indebted to the Atomic Energy Research Establishment, Harwell) followed the procedure described in Part V (*J.*, 1951, 3047). The results are shown in Table 1. The total glutamic acid

TABLE 1.

Synthetic mixture	Total glutamic acid hydrochloride present (g.)	L-[^{15}N]Glutamic acid hydrochloride added, g.	Atoms-% excess ^{15}N	DL-Glutamic acid hydrochloride isolated: No. of cryst.	Atoms-% excess ^{15}N	Total glutamic acid hydrochloride found (%)
A	0·7308	0·1036	14·956	5	1·869	99·25
				6	1·869, 1·872	99·20
				7	1·865, 1·865	99·50
						Mean 99·3
B	0·7051	0·0998	14·956	5	1·864, 1·865	99·37
				6	1·863, 1·862	99·48
				7	1·869, 1·866	99·19
						Mean 99·3
C	0·6450	0·1000	14·998	5	2·021, 2·028	99·35
				6	2·030	99·06
				7	2·024, 2·023	99·43
						Mean 99·3
D	0·6870	0·0892	14·998	5	1·737	99·09
				6	1·731, 1·734	99·40
				7	1·736, 1·738	99·13
						Mean 99·2
E	2·0052	0·3485	15·214	4	2·266	99·34
				5	2·266, 2·268	99·26
				6	2·265	99·35
						Mean 99·3

found in each experiment is 99·2—99·3% of the theoretical amount. From the close agreement with the result of Experiment *E*, in which the L-glutamic acid hydrochloride used in this work was itself analysed by this method, it seems likely that the accuracy may be slightly greater than these figures suggest.

As in the determination of the L-isomer, it is important to establish the purity of the isolated sample. Differential solubility tests (Part III, *J.*, 1951, 1279; Part IV, *ibid.*, p. 1745) will not detect the presence of a slight excess of one enantiomorph in the racemate, since the D- and the L-form dissolve independently, but they will detect other impurities in the normal manner. Optical-rotation measurements will then give satisfactory evidence of optical purity, when the absence of foreign contaminants has been established. It is however a great advantage of this procedure that for most applications even gross contamination of the racemate by the L-isomer has a negligible effect on the analysis. For example, if 5% of the glutamic acid is originally present as the D-form, racemisation is 95% complete, and the isotopic dilution is 1 : 10, it may readily be calculated that the presence in the isolated racemate of 5% of the L-isomer would result in an additional error of only 0·02%.

The total glutamic acid obtained on hydrolysis of a sample of gliadin (kindly supplied by Professor A. C. Chibnall) was determined by this method and the results are shown in Table 2. The mean value of 45·8 g. of dry, ash-free protein compares with the corresponding figure of 44·1 g. for the L-isomer from the same sample (Part V, *loc. cit.*), the difference

TABLE 2.

Experiment	Gliadin, g.	L-[^{15}N]Glutamic acid hydrochloride added, g.	Atoms-% excess ^{15}N	DL-Glutamic acid hydrochloride isolated: No. of cryst.	Atoms-% excess ^{15}N	Total glutamic acid found, G. per 100 g. of gliadin *	N, % of protein-N
(i)	1·5176	0·0598	14·810	4	1·061	45·83	24·64
				5	1·062, 1·060	45·85	24·65
				6	1·061, 1·060	45·87	24·66
					Mean	45·85	24·65
(ii)	1·3332	0·0728	14·810	4	1·435, 1·431	45·76	24·60
				5	1·434, 1·436	45·70	24·57
				6	1·434	45·73	24·59
					Mean	45·73	24·59
				Mean of experiments (i) and (ii):		45·8	24·62

* Calc. for dry, ash-free protein.

(1·7 g.) representing D-glutamic acid in the hydrolysate. This is remarkably close to the estimate (1·85 g.) based on optical-rotation measurements of fractions isolated by the gravimetric method by Chibnall and his colleagues (*J. Int. Soc. Leather Trades' Chem.*, 1946, **30**, 11). This amount may of course arise from racemisation during hydrolysis, a point that is now under investigation.

EXPERIMENTAL

Determination of the Total Glutamic Acid in Synthetic Mixtures.—(*A*) A solution of L-glutamic acid hydrochloride (0·7186 g.), DL-glutamic acid hydrochloride (0·0122 g.), and L-[^{15}N]-glutamic acid hydrochloride (0·1036 g.) in water (80 c.c.) was made alkaline to phenolphthalein paper with 5N-sodium hydroxide. Sodium carbonate (3·27 g.) was added and the solution was cooled to 0—2°. Benzoyl chloride (4·8 c.c.) was added, and the reaction mixture stirred vigorously for 4½ hours, after which the solution still gave a faintly positive ninhydrin test. Further additions of sodium carbonate (0·82 g.) and benzoyl chloride (1·1 c.c.) were made; stirring was continued for another 3 hours, a negative ninhydrin test being then obtained. When the solution had regained room temperature, acetic anhydride (60 c.c.) was added and the mixture was left overnight. A further volume of acetic anhydride (60 c.c.) was then added, and the solution left for 30 hours, after which it was evaporated to dryness below 50° under reduced pressure. The residual white solid was dissolved in water (40 c.c.), made acid to Congo-red with 5N-hydrochloric acid, and again evaporated to dryness *in vacuo*. The residue

was extracted with dried acetone, and the extract filtered and evaporated to dryness under reduced pressure, leaving a white solid which was refluxed for 4½ hours with 15% hydrochloric acid (45·5 c.c.). On cooling of the solution, benzoic acid separated and was removed by extraction with benzene. The aqueous layer was evaporated to dryness under reduced pressure; the residue was dissolved in a small volume of water, treated with charcoal, filtered, and concentrated to small bulk. The solution was saturated with hydrogen chloride at 0°. After being kept overnight in the cold, a crystalline mass separated and was filtered off, washed, and dried (0·55 g.); it had $[\alpha]_D^{18}$ +0·45° (*c*, 3·0 in 5% hydrochloric acid).

The crude DL-glutamic acid hydrochloride was recrystallised in all-glass apparatus, the first fraction which should contain any unchanged L-glutamic acid hydrochloride being rejected. The second fraction was filtered off through sintered-glass, washed, and recrystallised. Crystallisation was repeated 7 times and portions from each crystallisation were powdered and transferred to a vacuum-desiccator containing calcium chloride and sodium hydroxide pellets.

Differential-solubility tests for purity were carried out on the later fractions by the vapour-pressure method described in Part III (*J*, 1951, 1279). After the fourth crystallisation the product had no observable rotation (*c*, 1·0 in 5% hydrochloric acid).

No. of crystallisations	4	5	6	7
Yield (based on crude wt.), %	67	53	45	42
V. p. difference (mm. of oil)	4	3	3	3

(*B*) A solution of L-glutamic acid hydrochloride (0·6939 g.), DL-glutamic acid hydrochloride (0·0112 g.), and L-[^{15}N]glutamic acid hydrochloride (0·0998 g.) in water (75 c.c.) was benzoylated and racemised as described for synthetic mixtures *A*. DL-Glutamic acid hydrochloride (0·49 g.; $[\alpha]_D^{17}$ +0·5°, *c*, 2·5 in 5% hydrochloric acid) was isolated and crystallised seven times in all, in the usual manner.

No. of crystallisations	5	6	7
Yield (based on crude wt.), %	66	58	49
V. p. difference (mm. of oil)	3	4	3

(*C*) The mixture contained L-glutamic acid hydrochloride (0·6345 g.), DL-glutamic acid hydrochloride (0·0105 g.), L-[^{15}N]glutamic acid hydrochloride (0·1000 g.), L-aspartic acid hydrochloride (0·08 g.), and L-lysine hydrochloride (0·015 g.).

The mixture was benzoylated and racemised in the usual manner. On completion of the hydrolysis of the *N*-benzoyl-DL-glutamic acid with 15% hydrochloric acid and removal of the free benzoic acid, the aqueous layer was evaporated to dryness, redissolved in water (20 c.c.), made acid to Congo-red, and treated with a solution of ether-soluble phosphotungstic acid (3·5 g. in 2 c.c. of water) at 70° for the removal of basic amino-acids; the amino-dicarboxylic acids were extracted by using the anion-exchange resin Amberlite IR-4B (both procedures were as described in Part V, *J*, 1951, 3047). DL-Glutamic acid hydrochloride (0·45 g.; $[\alpha]_D^{21}$ +0·75°, *c*, 2·0 in 5% hydrochloric acid) was finally isolated and crystallised 7 times from 5N-hydrochloric acid as described in the previous experiments.

No. of crystallisations	5	6	7
Yield (based on crude wt.), %	58	44	39
V. p. difference (mm. of oil)	4	3	—

(*D*) A solution of the mixture containing L-glutamic acid hydrochloride (0·6743 g.), DL-glutamic acid hydrochloride (0·0127 g.), L-[^{15}N]glutamic acid hydrochloride (0·0892 g.), L-aspartic acid hydrochloride (0·08 g.), L-lysine hydrochloride (0·01 g.), DL-alanine (0·03 g.), L-tyrosine (0·01 g.), and glycine (0·01 g.) was treated as described for mixture *C*, and DL-glutamic acid hydrochloride (0·46 g.; $[\alpha]_D^{20}$ + 0·6°, *c*, 3·0 in 5% hydrochloric acid) was isolated and crystallised 7 times in all.

No. of crystallisations	5	6	7
Yield (based of crude wt.), %	60	52	45
V. p. difference (mm. of oil)	5	3	4

(*E*) L-Glutamic acid hydrochloride (2·0052 g.) and L-[^{15}N]glutamic acid hydrochloride (0·3485 g.) were dissolved in water (60 c.c.). The analytical procedure followed that for mixture *A*, yielding 1·5 g. of crude DL-glutamic acid hydrochloride, which was crystallised 6 times.

No. of crystallisations	4	5	6
Yield (based on crude wt.), %	58	52	45
V. p. difference (mm. of oil)	3	4	3

The isolated samples from each experiment were converted into nitrogen by Rittenberg's method (" Preparation and Measurement of Isotopic Tracers," Edwards, Ann Arbor, Michigan, 1947). The mass-spectrometric determinations were carried out by Mr. Palmer and his colleagues at the Atomic Energy Research Establishment, Harwell. The $^{15}N : ^{14}N$ ratio was calculated from the relative intensity of the peaks at mass numbers 29 and 28, as in Part V (*loc. cit.*); corrections were similarly applied for air and carbon dioxide. The total glutamic acid hydrochloride in the original mixture (X) was calculated from the formula $X = A\ [(C_o/C) - 1]$, where A is the amount of L-[^{15}N]glutamic acid hydrochloride added and C_o and C are the atoms-% excess of ^{15}N in the added and isolated materials respectively. The results are shown in Table 1.

Determination of the Total Glutamic Acid in Gliadin.—The sample of gliadin had 17·69(9)% Kjeldahl-N, corrected for 9·8% of moisture and 0·86% of ash. It was from the same batch as that used in Part V (*loc. cit.*).

(i) Gliadin (1·5176 g.) was treated with concentrated hydrochloric acid (8·12 c.c.) at room temperature for 18 hours, complete dissolution occurring. Water (6·2 c.c.) was added and the solution was then boiled under reflux for 24 hours. L-[^{15}N]Glutamic acid hydrochloride (0·0598 g.) was added and the heating was continued for a further hour. After repeated evaporation *in vacuo* at 50° to remove excess of acid, the product was benzoylated and then racemised in the manner described above. DL-Glutamic acid hydrochloride (0·5 g.; $[\alpha]_D^{20}$ + 0·75°, *c*, 2·0 in 5% hydrochloric acid) was isolated as previously and crystallised 6 times in all. After the fourth crystallisation the product had no observable rotation (*c*, 0·8 in 5% hydrochloric acid).

No. of crystallisations	4	5	6
Yield (based on crude wt.), %	65	56	49
V. p. difference (mm. of oil)	4	3	3

(ii) In a duplicate experiment with 1·3332 g. of gliadin, 0·0728 g. of L-[^{15}N]glutamic acid hydrochloride was added; 0·48 g. of crude DL-glutamic acid hydrochloride was isolated and crystallised 6 times.

No. of crystallisations	4	5	6
Yield (based on crude wt.), %	52	47	39
V. p. difference (mm. of oil)	3	3	—

The subsequent procedure and calculation were as described above for the synthetic mixtures. The results are shown in Table 2.

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Department of Chemistry, Bristol University.
The Dyson Perrins Laboratory, Oxford University. [*Received, December 22nd*, 1951.]

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289. *The Synthesis of Conjugated Hexuronic Acids.*

By C. A. Marsh.

Hexosides in neutral aqueous solution were converted by gaseous oxygen in the presence of a platinum catalyst into the corresponding conjugated hexuronic acids. By this method, (−)-menthyl-α- and -β-D-glucuronosides, and methyl-α- and -β-D-galacturonosides and -D-mannuronosides, were prepared, but attempts to oxidise phenyl-α- and -β-D-glucosides failed. The same procedure was used to oxidise α- and β-glucose-1 phosphate to the corresponding glucuronic esters, but the β-compound was not obtained in a pure state. The method appears to be specific for the oxidation of primary alcohol groups to carboxyl in sugars in which the reducing group has been protected by conjugation with an alcohol or by esterification.

It has been reported that glycosides can be oxidised to conjugated hexuronic acids by dinitrogen tetroxide (Maurer and Drehfahl, *Ber.*, 1942, **75**, 1489; Hardegger and Spitz, *Helv. Chim. Acta*, 1949, **32**, 2165; 1950, **33**, 337; Peterman, U.S.P. 2 520 255, 2 520 256),

alkaline hypobromite (Bergmann and Wolff, *Ber.*, 1923, **56**, 1060; Smolenski, *Roczn. Chem.*, 1924, **3**, 153; Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994), hydrogen peroxide in the presence of traces of ferric salts (Smolenski, *loc. cit.*), and electrolytic oxidation (Niemann and Link, *J. Biol. Chem.*, 1934, **104**, 195). By all these methods the yields obtained were poor, owing to the general difficulty, particularly in aqueous media, of selective oxidation of the primary alcohol group to carboxyl. In the absence of a suitable, specific oxidising agent, methods of synthesis involving initial protection of all the secondary alcohol groups by conversion into acetoxy- or *iso*propylidenedioxy-groups have generally been used (see Smith, Stacey, and Wilson, *J.*, 1944, 131), although Ault, Haworth, and Hirst (*J.*, 1935, 517) oxidised 2 : 3-*iso*propylidene methyl-α-D-mannopyranoside to the corresponding mannuronic acid derivative with alkaline potassium permanganate.

The use of gaseous oxygen in neutral or mildly alkaline solution, in the presence of a platinum catalyst, for the preparation of the corresponding saccharic acids from D-glucose (Mehltretter, Rist, and Alexander, U.S.P. 2 472 168) and 2 : 3-*iso*propylidene L-sorbose (Merck and Co., U.S.P. 2 483 251) has very recently been extended to the synthesis of 1 : 2-*iso*propylidene D-glucuronic acid from the mono*iso*propylidene derivative of D-glucose (Fernandez-Garcia *et al.*, *El Crisol, Puerto Rico*, 1950, **4**, 40; *Chem. Abs.*, 1951, **45**, 555; Mehltretter, Alexander, Mellies, and Rist, *J. Amer. Chem. Soc.*, 1951, **73**, 2424). After mild acid hydrolysis, good yields of glucuronic acid, in the form of the γ-lactone, were obtained.

This method seemed applicable to the oxidation of hexosides to the corresponding conjugated hexuronic acids, since the former are more stable to acids than *iso*propylidene derivatives of the sugars (Freudenberg, Durr, and Hochstetter, *Ber.*, 1928, **61**, 1735). The compounds initially chosen for oxidation were (−)-menthyl-α- and -β-D-glucopyranosides, as the corresponding hexuronosides are only slightly soluble in water and are therefore easily isolated. Good yields of these hexuronosides were obtained. Attempts to oxidise phenyl-α- and -β-D-glucopyranosides in this way were unsuccessful; the trace of free phenol liberated by slight hydrolysis was apparently sufficient to render the catalyst completely inactive after a very short time. The preparation of the methyl-α- and -β-glycosides of D-galacturonic and D-mannuronic acids, however, presented no difficulty. In the preparation of methyl-α-D-galacturonoside it was found that gaseous oxygen could be replaced by dilute hydrogen peroxide, but the yield was lower. The methyl-α- and -β-D-mannuronosides were hydrolysed to D-mannuronic lactone, m. p. 188° (decomp.), $[\alpha]_D^{22}$ +92°, and m. p. 189—191° (decomp.), $[\alpha]_D^{20}$ +89° respectively, whereas Ault, Haworth, and Hirst (*loc. cit.*) give m. p. 143—144°, $[\alpha]_D^{20}$ +95°. According to Professor F. Smith (personal communication), this lactone exists in two crystalline forms having identical optical rotations, the higher-melting isomer being more stable; an authentic specimen of the latter, m. p. 189° (decomp.), gave no depression when mixed with our products.

By catalytic oxidation of 3-methyl 1 : 2-*iso*propylidene D-glucose, 3-methyl 1 : 2-*iso*propylidene D-glucuronic acid was obtained as the sodium salt, which on hydrolysis yielded a product believed to be 3-methyl D-glucuronic acid. The method may thus be of importance in providing reference compounds for the identification of methylated glucuronic acids obtained in studies of polysaccharide structures (cf. Lythgoe and Trippett, *J.*, 1950, 1983; Overend, Shafizadeh, and Stacey, *J.*, 1951, 1487; Smith, *ibid.*, p. 2646).

The very mild nature of this reaction suggested that it might be applicable to the oxidation of the more labile glucose-1 phosphates. α-Glucuronic acid 1-phosphate was obtained, in the form of its tripotassium salt, without difficulty, but the product isolated from the oxidation of synthetic β-glucose-1 phosphate appeared to be unstable, and attempts at purification were unsuccessful. The properties of the crude product nevertheless indicate that it is largely composed of β-glucuronic acid 1-phosphate.

Synthetic (−)-menthyl-β-D-glucopyruronoside was identical in melting point and optical rotation with the urinary glucuronoside excreted after oral administration of (−)-menthol (Fromm and Clemens, *Z. physiol. Chem.*, 1901—2, **34**, 385), and this establishes the pyranose structure of the biosynthetic compound. Pryde and Williams (*Nature*, 1931, **128**, 187) have suggested from methylation studies that biosynthetic (+)-bornyl-β-D-glucuronoside is in the pyranose form, whereas Neuberg and Neimann (*Z. physiol.*

Chem., 1905, **44**, 114) claimed to have synthesised euxanthic acid and phenyl-β-D-glucuronoside, identical with the biosynthetic products, by condensation of acetobromoglucuronic lactone with the appropriate aglycones in the presence of potassium methoxide. This lactone has a furanose structure (Smith, *J.*, 1944, 584). The last-mentioned synthesis has not, however, been confirmed (Goebel and Babers, *J. Biol. Chem.*, 1933, **100**, 743).

Preliminary accounts of this work have already been published (Marsh, *Nature*, 1951, **168**, 602; *Biochem. J.*, 1951, **50**, xi). Barker, Bourne, and Stacey (*Chem. and Ind.*, 1951, **45**, 970) have independently described the oxidation of methyl-α- and -β-D-glucosides and α-glucose-1 phosphate by this method.

Experimental

(Determinations of carbon and hydrogen are by Drs. Weiler and Strauss. M. p.s are corrected.)

General Procedure.—The powdered platinum catalyst was prepared in aqueous suspension from Adams's platinum oxide catalyst (Johnson, Matthey, and Co., Ltd.) by hydrogenation at atmospheric pressure; it could be stored under water without undue loss of activity for about a week, after which its efficiency decreased. The aqueous solution or suspension of the hexoside or hexose ester was placed in a narrow cylindrical vessel tapering at the base to a coarse sintered-glass disc through which oxygen was forced from a cylinder into the reaction mixture; the vessel was heated by a water-bath. Vigorous mechanical stirring was necessary to disperse the heavy particles of catalyst. Small samples of liquid were withdrawn at frequent intervals for pH measurement, and neutrality was maintained by addition of alkali carbonate or bicarbonate, until no further pH change occurred. After removal of the catalyst, the product was treated as described for individual compounds. Evaporations of all aqueous solutions were conducted below 50° *in vacuo*.

(−)-*Menthyl-α-D-glucuronoside.*—A suspension of (−)-menthyl-α-D-glucoside (0·5 g.) and catalyst (0·1 g.) in water (80 c.c.) was oxidised at 65°, with addition of 0·5N-sodium hydrogen carbonate (3·0 c.c.) during 10 hours, after which no further pH change occurred, and all the glucoside had passed into solution. After removal of the catalyst, acidification with 2N-hydrochloric acid precipitated (−)-menthyl-α-D-glucuronoside (0·163 g., 31%), m. p. 135—136°. On recrystallisation from ethyl acetate–light petroleum (b. p. 100—120°), the dihydrate (0·144 g., 27%) melted at 141—142°, $[\alpha]_D^{21}$ +46° (*c*, 20 in alcohol). The mixed m. p. with an authentic specimen, m. p. 137—138° (Bergmann and Wolff, *loc. cit.*), was 137—140° (Found, for anhydrous compound: C, 58·3; H, 9·0. Calc. for $C_{16}H_{28}O_7$: C, 57·8; H, 8·5%). Bergmann and Wolff (*loc. cit.*) give m. p. 140° (decomp.), $[\alpha]_D^{18}$ +51·9° (in alcohol).

(−)-*Menthyl-β-D-glucuronoside.*—The oxidation of a solution of (−)-menthyl-β-D-glucoside (0·5 g.) (Treibs and Franke, *Annalen*, 1950, **570**, 76) in water (50 c.c.) with catalyst (0·1 g.) and neutralisation with sodium hydrogen carbonate (0·5N; 3·1 c.c.) was complete in 4 hours at 60° (−)-Menthyl β-D-glucuronoside was precipitated as the ammonium salt (0·3 g.) and converted into the free acid by Quick's method (*J. Biol. Chem.*, 1924, **61**, 667). Two recrystallisations from water yielded a pure product (*ca.* 30%), m. p. 75—77° (decomp. 114°), $[\alpha]_D^{21}$ −99° (*c*, 10 in alcohol). The mixed m. p. with a biosynthetic specimen, m. p. 79—80°, $[\alpha]_D^{21}$ −102° (*c*, 10 in alcohol), was 78—80°. Both compounds contained *ca.* $1\frac{1}{2}H_2O$ (Found, for anhydrous compound: C, 58·0; H, 8·5. Calc. for $C_{16}H_{28}O_7$: C, 57·8; H, 8·5%). According to Fromm and Clemens (*loc. cit.*), the biosynthetic material has m. p. 87—88°, but this appears to depend on the degree of hydration.

Methyl-α-D-galacturonoside.—(*a*) Oxidation of a solution of methyl-α-D-galactoside monohydrate (1·06 g.) in water (20 c.c.) with catalyst (0·1 g.), and neutralisation with N-sodium hydrogen carbonate (4·9 c.c.), was completed in 5 hours at 60°. The filtrate was made definitely alkaline with aqueous ammonia, and excess of basic lead acetate solution added, precipitating the lead salt of methyl-α-D-galacturonoside. The product was washed thrice with water (total 60 c.c.) on the centrifuge. The moist product, suspended in water (25 c.c.), was saturated with hydrogen sulphide at 0°, and after removal of lead sulphide evaporation of the colourless solution yielded a gum which crystallised when dried *in vacuo*. Recrystallisation from 95% alcohol gave methyl-α-D-galacturonoside dihydrate, m. p. 107—108° (0·441 g.), together with a second crop, m. p. 101—103° (0·075 g., total 42%). After a second recrystallisation the m. p. was 110°, with sintering at 105° and decomp. at 126°, $[\alpha]_D^{25}$ +128° (*c*, 2 in water) (Found, for anhydrous product: C, 41·0; H, 6·2. Calc. for $C_7H_{12}O_7$: C, 40·4; H, 5·8%). According to Morell and

Link (*J. Biol. Chem.*, 1933, **100**, 385), m. p. of the dihydrate is 112—114° with sintering at 109° and decomp. at 120° and $[\alpha]_D^{28}$ is +127·6° (*c*, 2—3 in water).

(*b*) To a solution of methyl-α-D-galactoside (1·06 g.) in water (40 c.c.) with catalyst (0·1 g.) was added 20-vols. hydrogen peroxide (50 c.c.) during 4 hours with stirring at 20°, the mixture being kept neutral with N-sodium hydrogen carbonate (3·8 c.c.). After filtration, the product was treated as in the preceding preparation, giving a crude gummy product (0·48 g.), which on recrystallisation from 95% alcohol had m. p. 105—107° (alone or mixed with the above product) (0·20 g., 16%), $[\alpha]_D^{20}$ +126° (*c*, 2 in water).

Methyl-β-D-galacturonoside.—Methyl-β-D-galactoside (0·97 g.) in water (20 c.c.) with platinum catalyst (0·1 g.) was completely oxidised in 6 hours at 65°, neutralisation being with N-sodium hydrogen carbonate solution (4·8 c.c.). The subsequent procedure was as for methyl-α-D-galacturonoside. The product, recrystallised from 95% alcohol, had m. p. 160—162° (0·247 g., 22%). A second recrystallisation gave the monohydrate, m. p. 163°, with sintering at 100—110°, decomp. at 182°, $[\alpha]_D^{25}$ −38° (*c*, 2·5 in water) (Found, for the anhydrous product: C, 40·3; H, 5·8. Calc. for $C_7H_{12}O_7$: C, 40·4; H, 5·8%). Morell, Baur, and Link (*ibid.*, 1935, **110**, 719) give m. p. 163—165°, decomp. at 180°, $[\alpha]_D^{25}$ −39·6° (*c*, 1·5—2·0 in water).

Methyl-α-D-mannuronoside.—Methyl-α-D-mannoside (3·88 g.) in water (50 c.c.) with catalyst (0·2 g.) was completely oxidised in 18 hours at 65°; 10% aqueous potassium carbonate (11·8 c.c.) was used for neutralization. Evaporation after removal of catalyst yielded a yellow gum, which solidified on addition of methyl alcohol (10 c.c.). The white crystalline potassium salt of methyl-α-D-mannuronoside (2·84 g.) decomposed slowly above 200°, with sintering at 100°, $[\alpha]_D^{20}$ +45° (*c*, 2 in water) (Found, for anhydrous compound: K, 15·3. Calc. for $C_7H_{11}O_7K$: K, 15·8%). Ault, Haworth, and Hirst (*loc. cit.*) give $[\alpha]_D^{17}$ +48° (*c*, 1·5 in water).

The potassium salt (1·8 g.), dissolved in water (2 c.c.), was treated at −5° with one equivalent of 25% perchloric acid, and alcohol (5 c.c.) was added. The filtered solution was evaporated to a colourless syrup, dissolved in alcohol (15 c.c.), and filtered from residual potassium perchlorate. Evaporation yielded a colourless gum which rapidly crystallised on addition of ether (1 c.c.) and then had m. p. 102—104° (1·25 g.; calc. on methyl-α-D-mannoside, 44%). Recrystallisation from alcohol–ether (2 : 1) gave the monohydrate, m. p. 106—107°, $[\alpha]_D^{20}$ +62° (*c*, 2 in water) (Found, for anhydrous compound: C, 41·0; H, 6·1. Calc. for $C_7H_{12}O_7$: C, 40·4; H, 5·8%). Ault, Haworth, and Hirst (*loc. cit.*) give m. p. 108°, $[\alpha]_D^{19}$ +65·6° (*c*, 1·2 in water).

Methyl-α-D-mannuronoside monohydrate (1·1 g.) on hydrolysis by Ault, Haworth and Hirst's method (*loc. cit.*) yielded a yellow gum (0·328 g.) which partly solidified. Recrystallisation from water gave a colourless product, m. p. 188° (decomp.) (0·26 g.), $[\alpha]_D^{22}$ +92° (*c*, 3 in water). This gave a strong Tollens reaction for uronic acid, and a positive test for reducing sugar (Found: C, 41·4; H, 4·6. Calc. for $C_6H_8O_6$: C, 40·9; H, 4·6%). The mixed m. p. with a specimen of mannuronic lactone, m. p. 189° (decomp.), supplied by Prof. F. Smith, was 187—190° (decomp.). Ault, Haworth, and Hirst (*loc. cit.*) give $[\alpha]_D^{20}$ +95° (*c*, 3 in water).

Methyl-β-D-mannuronoside.—Methyl-β-D-mannoside *iso*propanol solvate (1·68 g.) (Isbell and Frush, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 125), heated at 100° (6 hours), gave the solvent-free product (1·06 g.) as a colourless gum; the solution of this in water (30 c.c.) with catalyst (0·2 g.) was oxidised at 70°, and potassium carbonate solution (0·75N; 6·9 c.c.) added as necessary; no further pH change occurred after 6 hours. The filtered solution was evaporated to a syrup, from which a gum was precipitated on addition of methyl alcohol (15 c.c.). After 5 hours at 0° the *potassium* salt of methyl β-D-mannuronoside had solidified and was filtered off and dried *in vacuo* (1·12 g.). Precipitation from water with methyl alcohol gave the product as a yellowish, very deliquescent solid (0·78 g.), decomp. above 160°, $[\alpha]_D^{20}$ +15° (*c*, 6 in water) (Found, for anhydrous product: K, 16·0. $C_7H_{11}O_7K$ requires K, 15·8%). The neutral solution in water gave a strong Tollens test for uronic acid; the reaction for reducing sugar was only positive after hydrolysis with 3N-hydrochloric acid (5 minutes at 100°).

The potassium salt (0·160 g.), dissolved in water (2 c.c.), was converted into the free acid as for the corresponding α-isomer (see above). The reaction product, after removal of potassium perchlorate, was evaporated to a syrup which yielded a white gum on addition of alcohol (3 c.c.); this hardened to a solid (88 mg.) after 12 hours at 0° (Found, for anhydrous product: C, 39·6; H, 5·7. $C_7H_{12}O_7$ requires C, 40·4; H, 5·8%), $[\alpha]_D^{19}$ +25° (*c*, 2 in water). The strongly acid aqueous solution of *methyl-β-D-mannuronoside* gave a Tollens reaction for uronic acid, and the test for reducing sugar was only positive after hydrolysis with N-hydrochloric acid (5 minutes at 100°). Attempted recrystallisation from water–alcohol yielded a gum which on being dried *in vacuo* gave slightly positive tests for reducing sugar. The methyl-β-D-mannuronoside thus appears to be readily hydrolysed in aqueous solution.

Crude methyl-β-D-mannuronoside (0·11 g.) was hydrolysed with 2·5% hydrochloric acid to D-mannuronic lactone, m. p. and mixed m. p. 179—181° (decomp.) (28 mg.), $[\alpha]_D^{20}$ + 89° (*c*, 3 in water).

3-Methyl 1 : 2-iso*Propylidene Glucuronic Acid.*—A solution of 3-methyl 1 : 2-*iso*propylidene glucose (0·59 g.) (Vischer and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 1332) in water (15 c.c.) with catalyst (0·1 g.) was oxidised at 60°, N-sodium hydrogen carbonate (2·6 c.c.) being used for neutralization; the reaction was complete in 1 hour. Evaporation of the filtered solution gave a yellowish gum; on dissolution of this in alcohol and precipitation with ether *sodium 3-methyl* 1 : 2-iso*propylidene glucuronate* was precipitated as an amorphous power, $[\alpha]_D^{21}$ −35° (*c*, 4 in water) (0·45 g., 69%) (Found : Na, 8·1. $C_{10}H_{15}O_7Na$ requires Na, 8·5%). This gave a strong Tollens reaction for uronic acid; the reaction for reducing sugar was only positive after hydrolysis with 0·5N-hydrochloric acid (1 minute at 100°).

A solution of the sodium salt (0·45 g.) in water (10 c.c.) was passed through a column of cation exchange resin (Amberlite 100), and glacial acetic acid (1 c.c.) added to the pale yellow solution. When kept at 70° the solution became less lævorotatory until after 24 hours the rotation was very slightly positive, and no further change occurred. Evaporation (charcoal) gave a yellow gum, which, dried *in vacuo* over potassium hydroxide, had $[\alpha]_D^{21}$ +6° (*c*, 5 in water) (0·30 g.). The strongly acid aqueous solution gave a strong Tollens test for uronic acid and a positive test for reducing sugar. Neither the free acid nor its alkali salts could be crystallised (cf. Levene and Meyer, *J. Biol. Chem.*, 1924, **60**, 173).

α-Glucuronic Acid 1-Phosphate.—A solution of α-glucose-1 (dipotassium phosphate) (0·336 g.) in water (20 c.c.) and catalyst (0·1 g.) was oxidised at 40—45°, with addition of 1% aqueous potassium carbonate (4·3 c.c.) to keep the pH at 7·5—9·0; no further reaction occurred after 5 hours. Evaporation of the filtered solution yielded a gum, which was dissolved in 50% aqueous methyl alcohol (3 c.c.); absolute methyl alcohol (1·5 c.c.) was added, precipitating an oil which rapidly crystallised at 0° (0·273 g.). Recrystallisation from aqueous methyl alcohol by the same procedure gave pure *tripotassium α-glucuronate 1-phosphate* as the dihydrate, $[\alpha]_D^{20}$ +51° (*c*, 2·4 in water), decomp. above 150°, with sintering at 100°. It gave a strong Tollens reaction for uronic acid; the reaction for reducing sugar was only positive after hydrolysis with 3N-hydrochloric acid (15 minutes at 100°) [Found : loss at 78°, 9·3. $C_6H_8O_{10}PK_3,2H_2O$ requires H_2O, 8·5. Found, for anhydrous compound : Total P, 7·75; inorganic P, <0·1; K (Abul-Fadl, *Biochem. J.*, 1949, **44**, 282), 29·6; glucuronic acid (Hanson, Mills, and Williams, *ibid.*, 1944, **38**, 274), 49. $C_6H_8O_{10}PK_3$ requires P, 7·98; K, 30·1; glucuronic acid, 50%].

Oxidation of β-*Glucose-1* (*Dipotassium Phosphate*).—The dibrucine salt of β-glucose-1 phosphate was prepared by the method of Wolfrom, Smith, Pletcher, and Brown (*J. Amer. Chem. Soc.*, 1942, **64**, 23), and converted into the dipotasium salt by addition of two equivalents of 10% aqueous potassium hydroxide; the final pH was 8·8. After 2 hours at 0° and removal of brucine, the solution was evaporated to dryness at 30°, and alcohol (30 c.c.) was added to redissolve residual brucine. The microcrystalline, deliquescent dipotassium salt (0·31 g.) was filtered off, dried *in vacuo*, and used without further purification. A solution in water (0·140 g., 15 c.c.) together with catalyst (0·1 g.) was oxidised at 50°, with addition of 1% aqueous potassium carbonate (2·1 c.c.) to keep the pH at 8—9; reaction ceased after 3 hours. The catalyst was removed, and the solution evaporated at 35° to a syrup, from which a gum was precipitated on addition of methyl alcohol (5 c.c.). After two further precipitations from aqueous solution with methyl alcohol the colourless gum gave a very deliquescent yellowish powder (0·086 g.) when dried *in vacuo* (Found, after drying at 78° : Total P, 8·36; inorganic P, 1·06; K, 27·7; glucuronic acid, 33%). The Tollens test for uronic acid was strong, and a positive test for reducing sugar was obtained only after hydrolysis with 3N-hydrochloric acid (5 minutes at 100°). Attempts to purify the product from methyl alcohol–water reduced the glucuronic acid content.

The author thanks Dr. G. A. Levvy for advice and encouragement during this work, and Dr. J. Conchie for preparing methyl-β-D-mannoside *iso*propanol solvate. Gifts of α-glucose-1 phosphate from Dr. W. J. Whelan, and of D-mannuronic lactone from Professor F. Smith, are gratefully acknowledged.

THE ROWETT RESEARCH INSTITUTE,
BUCKSBURN, ABERDEENSHIRE.

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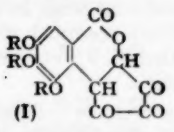
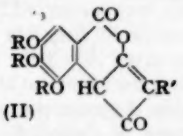
290. *Galloflavin. Part I.*

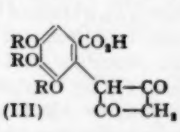
By R. D. Haworth and (Miss) J. M. McLachlan.

The preparation of galloflavin by aeration of alkaline solutions of gallic acid has been improved, the earlier degradative work of Herzig and his collaborators has been largely confirmed and extended, and new formulæ (IX; R = H) and (VII; R = H, R′ = CO_2H) have been proposed for galloflavin and *iso*galloflavin respectively. Two syntheses of 3-acetyl-4 : 5 : 6-trimethoxyphthalide (IV; R = Me), a degradation product of galloflavin, are described.

The yellow mordant dye, galloflavin, was first prepared by Bohn and Graebe (*Ber.*, 1897, **30**, 2327) by aeration of a solution of gallic acid in aqueous-alcoholic potassium hydroxide at 0°. The molecular formula, $C_{13}H_6O_9$, was proposed and crystalline tetra-acetyl and tetrachloroacetyl derivatives were described. Herzig and Tscherne (*Monatsh.*, 1904, **25**, 603) methylated galloflavin with diazomethane and later Herzig and Ruzicka (*ibid.*, 1910, **31**, 799) suggested that galloflavin was $C_{12}H_6O_8$ containing three phenolic hydroxyl groups and a lactone group. Methylation yielded a tetramethylgalloflavin, $C_{16}H_{14}O_8$, which on alkaline hydrolysis gave trimethyl*iso*galloflavin, $C_{15}H_{12}O_8$, containing a carboxyl group, esterified with methanolic hydrogen chloride to tetramethyl*iso*galloflavin, $C_{16}H_{14}O_8$. Methylation of tri- and tetra-methyl*iso*galloflavin first with methyl sulphate in alkaline solution, and then with diazomethane ruptured a lactone ring and gave a hexamethyl derivative, $C_{18}H_{20}O_9$, yielding, on hydrolysis, a dicarboxylic acid, $C_{16}H_{16}O_9$. On the basis of this experimental work, Herzig and Ruzicka suggested the presence of a carboxyl, a lactone, and three hydroxyl groups in *iso*galloflavin. They also showed that trimethyl*iso*-galloflavin and the dicarboxylic acid, $C_{16}H_{16}O_9$, were decarboxylated by heat and the products were more fully investigated later by Herzig and Waschler (*ibid.*, 1914, **35**, 77). This extension was made possible as these workers devised an improved preparation (28% yield) of *iso*galloflavin by the action of cold 10% potassium hydroxide on galloflavin. Methylation with diazomethane to tetramethyl*iso*galloflavin and subsequent alkaline hydrolysis gave trimethyl*iso*galloflavin, which was decarboxylated, and the product, $C_{14}H_{12}O_6$, subjected to regulated degradation with alkali. Heating with 5% aqueous-alcoholic potassium hydroxide gave a ketonic compound, $C_{13}H_{14}O_6$, which yielded 4 : 5 : 6-trimethoxyphthalide after treatment with 10% potassium hydroxide. In 1920, Herzig


(I)

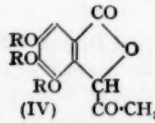

(II)


(III)

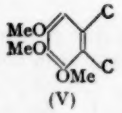
(*Annalen*, **421**, 247) interpreted these experimental findings on the basis of structures (I; R = H) and (II; R = H, R′ = CO_2H) for galloflavin and *iso*galloflavin, respectively, and the latter was derived from the former by a benzilic acid-type rearrangement. The ready decarboxylation of trimethyl*iso*galloflavin (II; R = Me, R′ = CO_2H) is understandable on the basis of the β-keto-acid structure and the subsequent conversion by alkaline hydrolysis into 4 : 5 : 6-trimethoxyphthalide was assumed to involve (*a*) hydrolysis of the lactone ring to a diketo*cyclo*butane derivative (III; R = Me), (*b*) fission of the latter to give (IV; R = Me) and formic acid, and (*c*) hydrolysis of (IV; R = Me) to 4 : 5 : 6-trimethoxyphthalide and acetic acid. The schemes relating to stage (*b*) are extremely improbable and unsatisfactory and in addition there are obvious stereochemical objections to structures such as (II).

As no research on the constitution of galloflavin has been reported since 1920, and in view of our interest in the oxidation of pyrogallol and other phenols, it was decided to reinvestigate the problem. The preparation and purification of galloflavin have been improved by the methods described in the Experimental section and the molecular formula,

$C_{12}H_6O_8$, confirmed. Galloflavin and its tetramethyl ether did not react with 2 : 4-dinitrophenylhydrazine or *o*-phenylenediamine, and the lack of ketonic activity is inconsistent with structure (I; R = Me). That a *cyclo*pentenedione system does in fact form ketonic derivatives is shown by the work of Koelsch and Geissmann (*J. Org. Chem.*, 1938, **3**, 480, 489) who prepared an oxime from 3 : 4-diphenyl*cyclo*pentene-1 : 2-dione and a quinoxaline from 3 : 4 : 5-triphenyl*cyclo*pentene-1 : 2-dione. Tetramethylgalloflavin contained no active hydrogen atoms, it was recovered from attempted reduction with hydrogen in presence of palladium–charcoal or platinic oxide catalysts, but oxidation with potassium permanganate in acetone solution gave 3 : 4 : 5-trimethoxyphthalic acid, thus



(IV)



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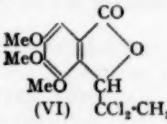


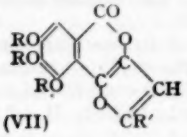
(VI)

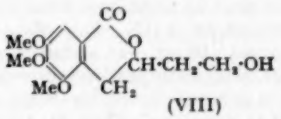
establishing the presence of the grouping (V). An improved preparation of *iso*galloflavin is reported in the Experimental section and new analytical data suggest that *iso*galloflavin separates as a monohydrate, but the triacetyl, and tri- and tetra-methyl derivatives were readily obtained in solvent-free states. The decarboxylation and alkaline degradation of trimethyl*iso*galloflavin, reported by Herzig and his colleagues, has been repeated and confirmed, and the constitution of the phthalide precursor (IV; R = Me) has been established synthetically. 4 : 5 : 6-Trimethoxyphthalide-3-carboxylic acid, prepared as described by Bargellini and Molina (*Atti R. Accad. Lincei*, 1912, **21**, ii, 146), was converted by thionyl chloride into the corresponding chloride, which reacted with dimethylcadmium to yield an oil, from which a small yield of ketonic material was extracted with Girard-T reagent. The ketone was recovered as an impure oil, which gave a 2 : 4-dinitrophenylhydrazone identical with the derivative prepared from the phthalide precursor (IV; R = Me). In a second attempted synthesis the 4 : 5 : 6-trimethoxyphthalide-3-carboxylic acid chloride was converted into the corresponding amide, which was dehydrated with phosphoric oxide in boiling toluene to yield 3-cyano-4 : 5 : 6-trimethoxyphthalide, but no ketonic material was obtained by reaction of this nitrile with methylmagnesium iodide. A satisfactory synthesis of (IV; R = Me) was, however, effected by condensing αα-dichloropropaldehyde (Moelants, *Bull. Soc. chim. Belg.*, 1943, **52**, 53) with methyl trimethylgallate in presence of 98% sulphuric acid; 3-1′ : 1′-dichloroethyl-4 : 5 : 6-trimethoxyphthalide (VI), obtained in 75% yields, was converted by careful treatment with 2N-sodium hydroxide into 3-acetyl-4 : 5 : 6-trimethoxyphthalide (IV; R = Me) identical with the phthalide precursor, and this was converted into 3-1′ : 1′-dichloroethyl-4 : 5 : 6-trimethoxyphthalide (VI) by treatment with phosphorus pentachloride in toluene.

The positive identification of this degradation product (IV; R = Me) encouraged further investigation on the structure of *iso*galloflavin, and our experiments support Herzig's view that it contained three phenolic hydroxyl groups, a lactone group, and a carboxyl group so situated that it could be readily eliminated on heating. But as the triacetyl and tri- and tetra-methyl derivatives of *iso*galloflavin gave no ketonic reactions with 2 : 4-dinitrophenylhydrazine or *o*-phenylenediamine, and as the tri- and tetra-methyl derivatives were recovered from attempted Clemmensen reduction, it was unlikely that the eighth oxygen atom was ketonic. There are very few references in the literature to *cyclo*butenones but Dixit (*J. Univ. Bombay*, 1935, **4**, 153) claims to have prepared 2-carboxy-3-*p*-hydroxyphenyl*cyclo*but-2-enone, which gave a semicarbazone and a phenylhydrazone, and, unlike *iso*galloflavin, was unstable to moisture and dilute alkali. Further, as tetramethyl*iso*galloflavin evolved no methane in the Zerewitinoff test, hydroxyl groups must be excluded. When trimethyl*iso*galloflavin was decarboxylated, the product, $C_{14}H_{12}O_6$, was non-ketonic and much less stable towards acids and alkalis; it was resinified by acids and degraded by alkali to the acetylphthalide derivative (IV; R = Me), described previously. In addition, the product, $C_{14}H_{12}O_6$, was easily reduced in presence of palladium–charcoal to a mixture, which was separated by chromatography into tetra-

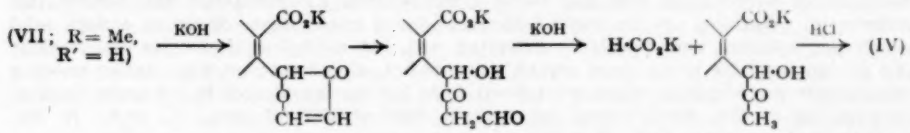
hydro- and hexahydro-derivatives melting at 83° and 84—85° respectively, and the former was converted into the hexahydro-derivative by further reduction. Both these reduction products were lactones, neither reacted with ketonic reagents, and the tetrahydro-derivative gave no methane with methylmagnesium iodide, but the hexahydro-derivative contained an active hydrogen atom and also yielded a crystalline 3 : 5-dinitrobenzoate. These results are inconsistent with both the *iso*galloflavin formula (II; R = H, R′ = CO_2H) and the structure (II; R = Me, R′ = H) for the decarboxylation product which should lead to a tetrahydro-derivative with secondary alcoholic properties, and the formation of the hexahydro-derivative would involve a rupture of the *cyclo*butane ring under exceptionally mild conditions.

Although it was abundantly clear that Herzig's formulæ were untenable, more satisfactory structures for galloflavin and its derivatives must still remain conjectural. In spite of this, however, we feel justified in proposing structures (VII; R = H, R′ = CO_2H), (VII; R = Me, R′ = CO_2Me), (VII; R = Me, R′ = CO_2H), and (VII; R = Me,

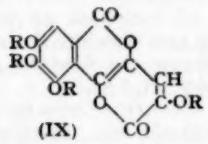

(VII)

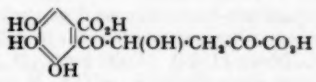

(VIII)

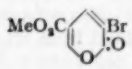
R′ = H) for *iso*galloflavin, tetramethyl*iso*galloflavin, trimethyl*iso*galloflavin, and the decarboxylation product, $C_{14}H_{12}O_6$, respectively, and a brief statement in support of these structures is advanced. The non-ketonic properties are explained, the tetrahydro-derivative mentioned above is interpreted as a tetrahydrofuran derivative, and its conversion into the hexahydro-derivative (VIII) containing an alcoholic group, corresponds to the usual hydrogenolysis of a benzyl ether. The furan-2-carboxylic acid structure (VII; R = H, R′ = CO_2H) for *iso*galloflavin and its derivatives is preferred to an analogous 3-carboxylic acid structure because it is consistent with (*a*) the ready decarboxylation of trimethyl*iso*galloflavin, (*b*) the influence of the 2-carboxyl group in stabilising the nucleus towards acids (as already indicated, trimethyl*iso*galloflavin is stable whereas the decarboxylation product is unstable to acids), and (*c*) the alkaline degradation of trimethyl-*iso*galloflavin, which is interpreted by the following scheme :


(VII; R = Me, R′ = H) KOH → KOH → HCl → (IV)

Although the furan ring is usually stable towards alkalis, the introduction of a 3-hydroxyl group causes instability (cf. Kohler, Westheimer, and Tischler, *J. Amer. Chem. Soc.*, 1936, **58**, 264) and the ring rupture employed in the scheme above corresponds exactly with ester or lactone hydrolysis. The mechanism accounts for the absorption of two equivalents of alkali, and the production of formic acid, and the increased stability of trimethyl*iso*galloflavin (VII; R = Me, R′ = CO_2H) finds an analogy in the work of Hoehn (*Iowa State Coll. J. Sci.*, 1936, **11**, 66), who showed that the normal instability of 3-hydroxyfuran is offset by the presence of a 2-carboxyl group.


(IX)


(X)


(XI)

On the basis of formula (VII; R = H, R′ = CO_2H) for *iso*galloflavin, the α-pyrone structure (IX; R = H) may be deduced for galloflavin. This is consistent with the

properties of the dye and the conversion into *iso*galloflavin *via* the hypothetical γ-diketonic intermediate product (X) is rational and analogous with the formation of furan-2 : 4-dicarboxylic acid by the action of alkali on (XI) (Feist, *Ber.*, 1901, **34**, 1992). Further work on these topics is in progress and a preliminary attempt to approach structure (VIII) from 4 : 5 : 6-trimethoxyindan-1-one, described in the Experimental section, indicates one of the synthetical routes which we are continuing to investigate.

Experimental

Galloflavin (IX; R = H).—Potassium hydroxide (67 c.c. of 28%) was added to gallic acid (25 g.) in water (500 c.c.) and ethyl alcohol (435 c.c.), and the solution was aerated at 0° for 5 hours. The precipitated yellow-green potassium salt was redissolved in water, then decomposed with 2N-hydrochloric acid in a nitrogen atmosphere, and the galloflavin (10 g.) collected, washed, and dried. A specimen was sublimed at 0·005 mm. (bath-temp., 220°); aggregates of small, stout, pale yellow prisms (Found: C, 51·5; H, 2·0. Calc. for $C_{12}H_6O_8$: C, 51·8; H, 2·2%) were obtained which decomposed at 290°. The alkaline filtrate from the potassium salt gave an additional small yield on further aeration.

Tetramethylgalloflavin (IX; R = Me).—An ethereal solution of diazomethane, prepared from nitrosomethylurea (10 g.), was added to a suspension of galloflavin (10 g.) in ether (50 c.c.). After 12 hours, tetramethylgalloflavin was collected; it crystallised from glacial acetic acid or amyl acetate in pale yellow needles (10 g.), m. p. 236—237° [Found: C, 57·2; H, 4·3; OMe, 36·6. Calc. for $C_{12}H_2O_4(OMe)_4$: C, 57·5; H, 4·2; OMe, 37·1%].

Oxidation of Tetramethylgalloflavin.—Potassium permanganate (75 c.c. of 2%) was added gradually with shaking to a suspension of tetramethylgalloflavin (0·5 g.) in acetone (12·5 c.c.). After a further 2 hours' shaking, the mixture was set aside overnight and then treated with a slight excess of sulphur dioxide. The solution was made strongly alkaline, evaporated to a small bulk, acidified with concentrated hydrochloric acid, and continuously extracted with ether for 6 hours. The dried extract was evaporated, and the residue sublimed at 0·3 mm. (bath-temp., 140—160°). The sublimate was triturated with chloroform and the insoluble crystals were collected and identified as oxalic acid. The chloroform filtrate was evaporated and the pale yellow residue, after two crystallisations from ether, gave colourless needles, m. p. 143—144°, which gave no depression with a synthetic specimen of 3 : 4 : 5-trimethoxyphthalic anhydride, m. p. 144—145°.

iso*Galloflavin* (VII; R = H, R′ = CO_2H).—A solution of galloflavin (10 g.) in 10% potassium hydroxide (175 c.c.) rapidly became dark, and after 45 minutes at room temperature concentrated hydrochloric acid was added carefully until the precipitate first formed just redissolved. Warming on the water-bath precipitated crude *iso*galloflavin as a dark solid which was collected and repeatedly extracted with hot methyl alcohol. The pale residue (4·8 g.) was insoluble in the usual organic solvents but, after treatment with boiling water, a *monohydrate* was obtained which crystallised from hot methyl alcohol in colourless needles, decomposing at 275—280° (Found, on material dried at 130°/0·5 mm.: C, 48·6; H, 2·6. $C_{12}H_6O_8,H_2O$ requires C, 48·7; H, 2·7%).

Triacetyl*iso*galloflavin (III; R = Ac, R′ = CO_2H), prepared by the action of acetic anhydride and sodium acetate on the monohydrate, crystallised from methyl alcohol in colourless silky needles, m. p. 223° (decomp.)[Found: C, 53·7; H, 3·1. Calc. for $C_{12}H_3O_5(OAc)_3$: C, 53·5; H, 3·0%], which did not react with 2 : 4-dinitrophenylhydrazine.

Tetramethyl*iso*galloflavin (VII; R = Me, R′ = CO_2Me), prepared by the action of diazomethane on an ethereal suspension of the monohydrate, separated from ethyl alcohol in colourless needles, m. p. 233—234° (Found: C, 57·5; H, 4·2. Calc. for $C_{16}H_{14}O_8$: C, 57·5; H, 4·2%), which did not react with 2 : 4-dinitrophenylhydrazine or with hydrogen in presence of a palladium–carbon catalyst, and gave a negative Zerewitinoff test.

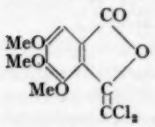
Trimethyl*iso*galloflavin (VII; R = Me, R′ = CO_2H), prepared by hydrolysis of tetramethyl*iso*galloflavin with potassium hydroxide as described by Herzig and Waschler (*loc. cit.*), separated from ethyl alcohol in colourless needles, m. p. 259—260° (Herzig and Waschler give m. p. 255—258°) (Found: C, 56·4; H, 3·9. Calc. for $C_{15}H_{12}O_8$: C, 56·3; H, 3·8%).

*Decarboxylation of Trimethyl*iso*galloflavin* (VII; R = Me, R′ = CO_2H).—Trimethyl*iso*galloflavin (1 g.) and copper powder (0·1 g.) were heated at 280° for 10 minutes. Distillation at 15 mm. (bath-temp., 280°) gave a yellow oil, which solidified on cooling; the product (VII; R = Me, R′ = H) crystallised from methyl alcohol in colourless needles (0·8 g.), m. p. 130—132° (Herzig, *Monatsh.*, 1910, **31**, 799, gives m. p. 130—134°) (Found: C, 61·5; H, 4·5. Calc.

for $C_{14}H_{12}O_6$: C, 60·9; H, 4·3%), which gave a negative Zerewitinoff test and failed to react with 2 : 4-dinitrophenylhydrazine.

Catalytic Reduction of $C_{14}H_{12}O_6$ (VII; R = Me, R′ = H).—A solution of the decarboxylation product (VII; R = Me, R′ = H) (0·47 g.) in ethyl alcohol was shaken with 25% palladium–charcoal (0·04 g.) in hydrogen for 6 hours at room temperature; 55 c.c. of hydrogen were absorbed. The mixture was then heated to 50° and the shaking continued for a further 12 hours, an additional 54 c.c. of hydrogen being taken up. After removal of the catalyst, concentration of the solution gave a small quantity (0·02 g.) of unchanged (VII; R = Me, R′ = H) and distillation of the residual oil (0·46 g.) at 0·007 mm. gave two fractions (*a*) and (*b*) with b. p. 215° and 230° (bath-temp.), respectively. Fraction (*a*) crystallised from ether in colourless prisms (0·04 g.), m. p. 83° (Found: C, 60·0; H, 5·7. $C_{14}H_{16}O_6$ requires C, 60·0; H, 5·7%). This *tetrahydrofuran* derivative, which gave a negative Zerewitinoff test and failed to react with 3 : 5-dinitrobenzoyl chloride and ketonic reagents, was insoluble in cold, but soluble in hot sodium hydroxide solution; it was recovered by acidification of the hot alkaline solution. A solution of fraction (*b*) (0·29 g.) in benzene (20 c.c.) was adsorbed on a column of alumina (12 g.) and eluted successively with benzene (75 c.c.), benzene–ether (9 : 1) (40 c.c.), benzene–ether (1 : 1) (100 c.c.), ether (50 c.c.), ether–acetone (9 : 1) (60 c.c.), and ether–acetone (1 : 1) (60 c.c.). The first five eluates were discarded but the sixth gave the *hexahydro*-derivative (VIII) (0·2 g.), which separated from ether in large colourless plates, m. p. 84—85° (Found: C, 59·6; H, 6·6; active hydrogen, 0·98. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%) depressed to 75—78° when mixed with a sample of the tetrahydrofuran derivative, m. p. 83°, described above. The hexahydro-derivative (VIII) had no ketonic properties, it was insoluble in cold but soluble in hot sodium hydroxide solution, and it was recovered by acidifying the solution and warming gently. The 3 : 5-*dinitrobenzoate*, prepared by reaction with 3 : 5-dinitrobenzoyl chloride and pyridine for 10 days at room temperature, separated from benzene in stout colourless prisms, m. p. 147·5—148·5° (Found: C, 53·3; H, 4·3; N, 6·0. $C_{21}H_{20}O_{11}N_2$ requires C, 52·9; H, 4·2; N, 5·9%). This hexahydro-derivative was also prepared from the tetrahydrofuran derivative (50 mg.) by reduction in presence of 10% palladium–charcoal (50 mg.) in ethyl alcohol at room temperature for 12 hours.

3-*Acetyl*-4 : 5 : 6-*trimethoxyphthalide* (IV; R = Me).—Prepared as described by Herzig and Tscherne (*loc. cit.*), this crystallised from methyl alcohol in colourless needles, m. p. 75—76° (Herzig and Tscherne, *loc. cit.*, give m. p. 74—77°) (Found: C, 58·9; H, 5·5. Calc. for $C_{13}H_{14}O_6$: C, 58·6; H, 5·3%), gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 203—204° (Found: C, 51·3; H, 4·3; N, 12·4. $C_{19}H_{18}O_9N_4$ requires C, 51·1; H, 4·0; N, 12·5%), and, on hydrolysis with warm 10% alcoholic potassium hydroxide (20 parts) for 20 minutes, yielded 4 : 5 : 6-trimethoxyphthalide, m. p. 134—135°, identical with a synthetic specimen prepared from trimethylgallic acid, formaldehyde, and concentrated hydrochloric acid. The ketone (IV; R = Me) (0·1 g.), phosphorus pentachloride (0·2 g.), and benzene (25 c.c.) were refluxed for 12 hours. After being washed first with water and then with sodium hydrogen carbonate solution, the benzene solution was dried and the solvent removed; 3-1′ : 1′-dichloroethyl-4 : 5 : 6-trimethoxyphthalide (VI), m. p. 110—112°, was obtained, identical with the synthetic product described below (p. 1588).



3-*Dichloromethylene*-4 : 5 : 6-*trimethoxyphthalide* (inset).—This *phthalide* was obtained during the preparation of 4 : 5 : 6-trimethoxyphthalide-3-carboxylic acid, by boiling 3-trichloromethyl-4 : 5 : 6-trimethoxyphthalide (1 g.) (Bargellini and Molina, *loc. cit.*) with 12% sodium hydroxide solution (8 c.c.) for 2 hours. The mixture was cooled, and the solid crystallised from ethyl alcohol; colourless needles, m. p. 145—146° (Found: C, 46·9; H, 3·8; Cl, 22·9. $C_{12}H_{10}O_5Cl_2$ requires C, 47·2; H, 3·4; Cl, 23·2%), were obtained which gave 4 : 5 : 6-trimethoxyphthalide-3-carboxylic acid on further refluxing with sodium hydroxide solution.

4 : 5 : 6-*Trimethoxyphthalide*-3-*carboxyamide*.—4 : 5 : 6-Trimethoxyphthalide-3-carboxylic acid (1·2 g.) was heated with thionyl chloride (10 c.c.), and after 2 hours excess of thionyl chloride was removed under reduced pressure and the last traces by evaporation with benzene. Addition of excess of aqueous ammonia to the residual acid chloride precipitated the *amide*, crystallising from alcohol in colourless needles (0·51 g.), m. p. 203—205° (Found: N, 5·3. $C_{12}H_{13}O_6N$ requires N, 5·2%).

3-*Cyano*-4 : 5 : 6-*trimethoxyphthalide*.—A solution of 4 : 5 : 6-trimethoxyphthalide-3-carboxyamide (1·8 g.) in toluene (40 c.c.) was refluxed for 12 hours with phosphoric oxide (1·8 g.). The mixture was decomposed with ice-water, and extracted several times with ether. The combined ether and toluene extracts were washed successively with water, sodium hydrogen carbonate

solution, and water, solvents were removed under reduced pressure, and the residual *nitrile* crystallised from ethyl alcohol; colourless needles (1 g.), m. p. 136—138° (Found: C, 57·8; H, 4·9; N, 5·7. $C_{12}H_{11}O_5N$ requires C, 57·8; H, 4·5; N, 5·6%), were obtained.

Synthesis of 3-*Acetyl*-4 : 5 : 6-*trimethoxyphthalide* (IV; R = Me).—(*a*) Cadmium chloride (5 g., dried at 120°) was added to the Grignard reagent prepared from magnesium (1·3 g.), methyl iodide (9 g.), and ether (200 c.c.). The mixture was stirred for 1 hour under nitrogen until a negative test was given with Michler's ketone. A toluene solution (50 c.c.) of the crude acid chloride obtained, as described above, by the action of thionyl chloride on 4 : 5 : 6-trimethoxyphthalide-3-carboxylic acid (3 g.) was now added, and after 3 hours at room temperature the mixture was decomposed with dilute hydrochloric acid at 0°. The product, isolated with ether as a dark viscous oil (1·4 g.), was taken up in alcohol (20 c.c.), refluxed for 1 hour with Girard-T reagent (1·5 g.) and glacial acetic acid (2 c.c.), and poured into an ice-cold sodium acetate solution. Non-ketonic material was removed with ether, and the aqueous layer was hydrolysed with cold hydrochloric acid and again extracted with ether. The washed and dried extract yielded an oil containing 3-acetyl-4 : 5 : 6-trimethoxyphthalide, which was isolated as the 2 : 4-*dinitrophenylhydrazone*, separating from alcohol in yellow needles, m. p. 202—203° (Found: C, 51·6; H, 4·3; N, 12·3. $C_{19}H_{18}O_9N_4$ requires C, 51·1; H, 4·0; N, 12·5%), undepressed on admixture with the 2 : 4-dinitrophenylhydrazone, m. p. 202—203°, from the ketone, $C_{13}H_{14}O_6$, prepared from galloflavin.

(*b*) αα-Dichloropropaldehyde (3 g.), prepared as described by Moelant (*loc. cit.*), methyl 3 : 4 : 5-trimethoxybenzoate (4 g.), and concentrated sulphuric acid (25 c.c.) were shaken for a few minutes and kept at room temperature for 40 hours. The mixture was decomposed with ice, and the sticky brown product crystallised from methyl alcohol, colourless prisms (3·6 g.), m. p. 110—112° (Found: C, 48·4; H, 4·2; Cl, 22·5. $C_{13}H_{14}O_5Cl_2$ requires C, 48·6; H, 4·4; Cl, 22·1%), being obtained. This 3-1′ : 1′-*dichloroethyl*-4 : 5 : 6-*trimethoxyphthalide* (VI) (0·2 g.) was boiled with 8% sodium hydroxide (3 c.c.) for a few minutes, the solution was acidified, heated on the water-bath for 30 minutes, and cooled, and 3-acetyl-4 : 5 : 6-trimethoxyphthalide (0·13 g.) was isolated with ether. Crystallisation from methyl alcohol yielded colourless needles, m. p. 74—75° (Found: C, 58·9; H, 5·5%), undepressed by admixture with the ketone, $C_{13}H_{14}O_6$, obtained from galloflavin. The 2 : 4-dinitrophenylhydrazone separated from ethyl alcohol in bright yellow needles, m. p. 202—203° (Found: C, 51·3; H, 4·3; N, 12·5%).

4 : 5 : 6-*Trimethoxyindan*-1-*one*.—A mixture of phosphoric oxide (4 g.) and β-(2 : 3 : 4-trimethoxyphenyl)propionic acid (1 g.) in benzene (20 c.c.) was refluxed for 1¼ hours and then decomposed with ice. The product (0·7 g.) isolated with ether had m. p. 75—82°, and was redissolved in ether, adsorbed on alumina (40 g.), and eluted with ether (90 c.c.), ether (30 c.c.), and ether–acetone (9 : 1) (60 c.c.). The first eluate yielded 4 : 5 : 6-*trimethoxyindan*-1-*one* (0·35 g.) which separated from light petroleum (b. p. 40—60°) in colourless needles, m. p. 80—81° (Found: C, 65·0; H, 6·2. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%). 2-*Benzylidene*-4 : 5 : 6-*trimethoxyindan*-1-*one* crystallised from alcohol in slender pale yellow needles, m. p. 159—160° (Found: C, 73·8; H, 5·8. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·8%). The last eluate yielded pale yellow needles, m. p. 165—166° (Found: C, 67·7; H, 5·8. $C_{24}H_{28}O_7$ requires C, 67·6; H, 6·1%), from methanol; this is probably the *anhydrobisindanone* derivative.

Ethyl 1-*Keto*-4 : 5 : 6-*trimethoxyindane*-2-*glyoxylate*.—A solution of 4 : 5 : 6-trimethoxyindanone (4 g.) and ethyl oxalate (2·63 g.) in alcohol (21 c.c.) was added to a solution of sodium (0·414 g.) in cold alcohol (2 c.c.). An orange sodium salt rapidly separated, and after 24 hours the mixture was decomposed with dilute sulphuric acid. *Ethyl* 1-*keto*-4 : 5 : 6-*trimethoxyindane*-2-*glyoxylate* was obtained as slender yellow needles (4 g.), m. p. 145—146° (Found: C, 59·2; H, 5·6. $C_{16}H_{18}O_7$ requires C, 59·2; H, 5·6%), by crystallisation from alcohol, but attempts to decarbonylate the ester were unsuccessful.

2-*Bromo*-4 : 5 : 6-*trimethoxyindan*-1-*one*.—Bromine (0·434 g.) in chloroform (6·5 c.c.) was added to a solution of the indanone (0·5 g.) in chloroform (5 c.c.) at 0°. After 1 hour the chloroform solution was washed with sodium hydrogen carbonate solution and dried, and the solvent removed. The residual *indanone* crystallised from methyl alcohol in colourless needles (0·65 g.), m. p. 92° (Found: C, 47·5; H, 4·2; Br, 26·9. $C_{12}H_{13}O_4Br$ requires C, 47·8; H, 4·3; Br, 26·6%).

2-*Cyano*-4 : 5 : 6-*trimethoxyindanone*, obtained in 75% yield by warming 2-bromoindan-1-one with potassium cyanide (2 parts) in alcohol (30 vols.) for 25 minutes, separated from methyl alcohol in colourless needles, m. p. 111—112° (Found: 62·9; H, 5·2; N, 5·6. $C_{13}H_{13}O_4N$ requires C, 63·1; H, 5·3; N, 5·7%).

2-*Cyano*-2-2′-*hydroxyethyl*-4 : 5 : 6-*trimethoxyindan*-1-*one*.—A solution of 2-cyano-4 : 5 : 6-

trimethoxyindan-1-one (0·335 g.), ethylene oxide (0·1 g.), and piperidine (1 drop) in alcohol (15 c.c.) was left for 4 weeks at room temperature. The solvent was removed under reduced pressure and the residue was taken up in ether, washed successively with water, dilute hydrochloric acid, sodium hydroxide and water, and dried, and the ether removed. The residue (0·2 g.) separated from alcohol in colourless needles, m. p. 149—150° (Found: C, 61·7; H, 6·2; N, 4·8. $C_{18}H_{17}O_5N$ requires C, 61·9; H, 5·8; N, 4·8%). Inferior yields of the *cyano*-compound were obtained when the piperidine catalyst was replaced by sodium ethoxide.

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THE UNIVERSITY, SHEFFIELD, 10. [*Received, January 14th*, 1952.]

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291. *The Stereochemistry of the 2-Aminocyclopentanols.*

By G. FODOR and J. KISS.

The stereochemical course of the reactions of the diastereoisomeric (±)-2-acylamino*cyclo*pentanols with hydrogen chloride and with thionyl chloride was investigated.

The *cis*-isomers (II) participated reversibly, without change of configuration, in both N ⟶ O acyl migration (II ⇌ III) and oxazoline formation (II ⇌ IV) whereas the *trans*-compounds (I) gave (III) and (IV) by irreversible reactions involving inversion of configuration.

The behaviour of the *trans*-acylamino*cyclo*pentanols thus conforms to that of derivatives of ephedrine, whereas the *cis*-isomers behave in a similar manner to the acyl derivatives of ψ-ephedrine.

OUR investigations of N ⟶ O acyl migrations in the isomeric 2-benzamido*cyclo*hexanols at 25° (Fodor and Kiss, *Nature*, 1949, **164**, 917) led to conclusions, as to the configuration of the diastereoisomers, similar to those reached by McCasland, Clark, and Carter (*J. Amer. Chem. Soc.*, 1949, **71**, 637) by other means. As, however, the stereospecific differences between the diasteroisomers disappear at 90°, because of the flexibility of the *cyclo*hexane ring, we then found it advisable to continue our investigations on more rigid ring systems.

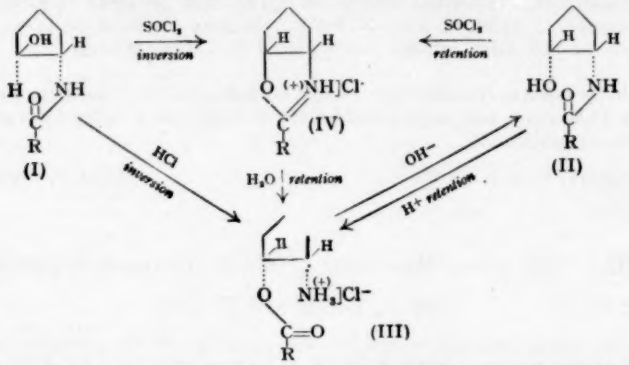
Meanwhile, McCasland and D. A. Smith (*ibid.*, 1950, **72**, 2190) have dealt with the geometry of the 2-amino*cyclo*pentonols in order to study the effect of configuration on the stereochemical behaviour. These workers prepared the *cis*-compound by tosylation and detosylation of the *trans*-isomer (Winstein *et al.*, *ibid.*, 1942, **64**, 2796; 1948, **70**, 812); although better results were achieved by application to the *cis*-oxazoline of the method described by Pfister, Robinson, Shabica, and Tischler (*ibid.*, 1949, **71**, 1101; cf. Fry, *J. Org. Chem.*, 1949, **14**, 887; Moersch and Moore, U.S.P. 2 513 346/1950).

They found that *cis*-2-amino*cyclo*pentyl *p*-nitrobenzoate, prepared from 2-*p*-nitrophenyl-*cis*-4 : 5-*cyclo*pentano-oxazoline, gave the 2-*p*-nitrobenzamido-alcohol by O ⟶ N acyl migration; they did not, however, examine the reverse, N ⟶ O acyl migration, or the action of thionyl chloride on the *cis*-2-acylamino*cyclo*pentanols.

We have obtained (±)-*trans*-2-benzamido- and -*p*-nitrobenzamido-*cyclo*pentanol (cf. I), and converted them, by the action of thionyl chloride, into the *cis*-isomers (cf. II). The *cis*- and *trans*-isomers were then treated under identical conditions with hydrogen chloride. The free and the bound hydrogen-ion concentrations, and therefore the conversion rate, could not be determined by acidimetric or potentiometric titration; the problem will be dealt with in detail later.

Treatment of (±)-*cis*-2-benzamido*cyclo*pentanol (II; R = Ph) in dioxan at 20° with 20 mols. of hydrogen chloride gave an 89% yield of (±)-*cis*-2-amino*cyclo*pentyl benzoate hydrochloride (III; R = Ph) besides 10% of an amorphous product. As expected (III; R = Ph) immediately reverted to (II; R = Ph) on treatment with alkali. Thus, in this series the N ⟶ O acyl migration was reversible as the configuration had been retained

(Welsh, *J. Amer. Chem. Soc.*, 1949, **71**, 3500; Fodor and Kiss, *Acta Chim. Acad. Sci. Hungar.*, 1951, 130). Under identical conditions the *trans*-alcohol (I; R = Ph) was unreactive. At 100° in a sealed tube both the *cis*- and the *trans*-alcohol gave (III; R = Ph) in yields of 78% and 72%, respectively, and it was not possible to convert the latter



back into the *trans*-alcohol (I; R = Ph); presumably the N ⟶ O acyl migration was in this case accompanied by inversion of configuration. It can be assumed that the mechanism postulated by Welsh (*loc. cit.*) for 2-acylamino-alcohols, based on Winstein's general theory (*inter al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 4669) is valid for this inversion. This observation led to a more practical preparation of *cis*-2-amino*cyclo*pentanol derivatives than the application of the thionyl chloride technique.

For solubility reasons further work was carried out on the *p*-nitrobenzamido-compounds; the extent and direction of the conversion at room temperature in this series resembled that of the benzamido-compounds. At higher temperatures the *cis*-alcohol (II; R = $C_6H_4{\cdot}NO_2$-*p*) underwent a 65% conversion into (III; R = $C_6H_4{\cdot}NO_2$-*p*) and gave also 10—18% of 2-chloro*cyclo*pentylamine of unknown configuration; the latter probably arose by a chlorination concomitant with the acyl migration, but a nucleophilic attack by chlorine ions on the 2-hydroxyoxazolidine intermediate cannot be excluded. The *trans*-amide (I; R = $C_6H_4{\cdot}NO_2$-*p*), on the other hand, gave about 87% of (III; R = $C_6H_4{\cdot}NO_2$-*p*) and approximately 12% of the *p*-nitrobenzoic acid salt.

The main product from the reaction of (II; R = $C_6H_4{\cdot}NO_2$-*p*) with thionyl chloride was the *cis*-oxazoline (IV; R = $C_6H_4{\cdot}NO_2$-*p*). That this reaction is accompanied by retention of configuration indicates that the oxazoline ring is formed from acylamino-alcohols containing a rigid ring, through a condensation of the diastereoisomer with spatially close functional groups, but by a nucleophilic attack in the isomer in which the groups are spacially opposed. The same is true for N ⟶ O acyl migration.

These findings are of interest; those for the *trans*-alcohols (I) are similar to our observations on ephedrine, norephedrine, and chloramphenicol, whereas the behaviour of the *cis*-compounds (II) agrees with that of the analogous derivatives of nor-ψ-ephedrine. With the results of other stereospecific reactions they support our concept of the *trans*-conformation of ephedrine and the *cis*-conformation of ψ-ephedrine (Fodor and Koczka, *J.*, 1952, 850; cf. Close, *J. Org. Chem.*, 1950, **15**, 1131).

The results also show that a *cis*-conformation of the hydroxy- and amino-groups can be inferred when the N ⟶ O acyl migration is reversible, whereas non-reversibility indicates a *trans*-conformation of the principal functions in these amino-alcohols. With alicyclic derivatives the configuration is similarly indicated.

Experimental

(±)-trans-2-*Amino*cyclo*pentanol*.—This was prepared by the method described by McCasland and Smith (*loc. cit.*), but without isolation of the epoxide, from 2-chloro*cyclo*pentanol (58 g.) and aqueous ammonia (1000 ml.; *d* 0·88); the amine hydrochloride (38 g., 48%) and unchanged chloro-compound (12 g.) were obtained.

Acyl Derivatives.—These were prepared as described by Leffler and Adams (*J. Amer. Chem. Soc.*, 1937, **59**, 2256) with benzoyl chloride and *p*-nitrobenzoyl chloride; the latter reagent, however, at 50° gave 2-p-*nitrobenzamido*cyclo*pentyl* p-*nitrobenzoate*, m. p. 170—172° (Found: N, 10·6. $C_{19}H_{17}O_7N_3$ requires N, 10·55%). Hydrolysis of this ester (3·1 g.) with N-sodium hydroxide (10 ml.) and ethanol (20 ml.) by Kunz's method gave the *p*-nitrobenzamido-alcohol.

(±)-cis- *and* -trans-2-*Benzamido*cyclo*pentanol*.—(*a*) These were obtained as described by McCasland and Smith (*loc. cit.*).

(*b*) Heating a dioxan (5 ml.) solution of the (±)-*trans*-benzamido-alcohol (I; R = Ph) (1 g.) with a 5N-solution (5 ml.) of hydrogen chloride in dioxan in a sealed tube for 2 hours at 100° gave the amino-benzoate hydrochloride (III; R = Ph), which was converted by O ⟶ N acyl migration into the *cis*-amide (II; R = Ph) (0·72 g., 72%).

(±)-2-p-*Nitrophenyl*-cis-4 : 5-cyclo*pentano-oxazolinium Chloride* (IV; R = $C_6H_4{\cdot}NO_2$-*p*).—(*a*) This salt, m. p. 159—161° (decomp.), was obtained by treatment of the *trans*-amido-alcohol (I; R = $C_6H_4{\cdot}NO_2$-*p*) with thionyl chloride in ethyl acetate (cf. McCasland and Smith, *loc. cit.*, who record m. p. 150—151°) (Found: N, 10·2; Cl^-, 12·8. Calc. for $C_{12}H_{12}O_3N_2$,HCl: N, 10·45; Cl^-, 13·2%).

(*b*) The (±)-*cis*-*p*-nitrobenzamido-alcohol (II; R = $C_6H_4{\cdot}NO_2$-*p*) (2 g.) in anhydrous dioxan (30 ml.) was treated with thionyl chloride (2 ml.) for 3 hours at 25°; light petroleum was then added. After 2 days the mixture was heated on the steam-bath for a few minutes, and the solution decanted from the oil and allowed to cool. The separated crystals had m. p. 116—120°, raised on crystallisation to 123—124°. Analysis suggested that these were 2-*chloro*-1-p-*nitrobenzamido*cyclo*pentane* (Found: C, 52·8; H, 5·3; N, 10·3; Cl, 12·0. $C_{12}H_{13}O_3N_2Cl$ requires C, 53·7; H, 4·85; N, 10·4; Cl, 13·2%). The oily residue was triturated with water (15 ml.); after removal of the deep-coloured crystals (1·03 g.; m. p. 128°) the aqueous solution was made alkaline and a second crop of crystals (0·52 g.; m. p. 133—135°) obtained. These were identified by mixed melting-point determination as (±)-2-*p*-nitrophenyl-*cis*-4 : 5-*cyclo*pentano-oxazoline (cf. IV; R = $C_6H_4{\cdot}NO_2$-*p*) (McCasland and Smith, *loc. cit.*). The picrate had m. p. 193—195° after recrystallisation from dry dioxan–light petroleum (Found: C, 46·4; H, 3·6; N, 15·3. Calc. for $C_{12}H_{12}O_3N_2$,$C_6H_3O_7N_3$: C, 46·8; H, 3·3; N, 15·2%) (McCasland and Smith, *loc. cit.*, record m. p. 210°). When the picrate was recrystallised from 96% alcohol the *picrate monohydrate* of 2-amino*cyclo*pentyl *p*-nitrobenzoate (III; $C_6H_4{\cdot}NO_2$-*p*) was obtained; this had m. p. 166—168° (decomp.) (Found: C, 43·3; H, 3·95. $C_{12}H_{14}O_4N_2$,$C_6H_3O_7N_3$,H_2O requires C, 43·4; H, 3·8%). This picrate monohydrate was also obtained by treatment of the amino-ester hydrochloride with sodium picrate.

(±)-cis-2-*Amino*cyclo*pentyl* p-*Nitrobenzoate Hydrochloride* (III; R = $C_6H_4{\cdot}NO_2$-*p*).—(a) When the *cis*-oxazolinium chloride (IV; R = $C_6H_4{\cdot}NO_2$-*p*) (0·5 g.) was heated with wet dioxan (16 ml.), and light petroleum (10 ml.) then added, (III; R = $C_6H_4{\cdot}NO_2$-*p*) was obtained as needles (0·485 g.), m. p. 185—187° raised to 191—192° (decomp.) on recrystallisation from

Amide, 10^{-3} mole	Dioxan, c.c.	Mole HCl/mole amide	Conditions	Products from *cis*-isomer: unchanged alcohol, %	Products from *cis*-isomer: amino-ester salt, %	Products from *trans*-isomer: unchanged alcohol, %	Products from *trans*-isomer: amino-ester salt, %	Other products, %
cis- (II; R = $C_6H_4{\cdot}NO_2$-p) *and* trans-2-p-*nitrobenzamido*cyclo*pentanol* (I; R = $C_6H_4{\cdot}NO_2$-p)								
0·88	5	1·25	A	36·4	42·2	100	—	—
0·88	5	6·25	A	—	48·2	99·4	—	12·7 *
0·88	5	31·25	A	—	82·5	97·6	—	10·4 *
4	20	5·0	B	—	79·3	84·0	10·6	17·8 *
4	10	5·0	C	—	—	—	84·0	12·0 †
5	22	4·4	C	—	81·5	—	—	18·2 *
cis- (II; R = Ph) *and* trans-2-*benzamido*cyclo*pentanol* (I; R = Ph)								
1	—§	10	A	—	62·7	93·0	—	34·5 ‡
4·9	5	5	C	—	—	—	72·0	26·0 ‡
1	3	3·1	C	—	78·0	—	—	15·0 ‡
1	3	20·0	A	—	89·0	—	—	10·0 ‡
2·15	6	1·15	A	—	—	82·0	—	16·0 ‡
2·15	6	19·0	A	—	—	75·0	—	23·0 ‡

Conditions: A, 15 hours at 20°; B, 2 hours at 100°; C, 2 hours at 100° in a sealed tube.

* Chloro-compound from the *cis*-isomer.
† *p*-Nitrobenzoic acid salt.
‡ Amorphous product.
§ In ethanol (5 c.c.).

dioxan (40 ml.)–light petroleum (16 ml.). McCasland and Smith (*loc. cit.*) record m. p. 168° for their sample of this compound, prepared by the action of dilute hydrochloric acid on (IV; R = $C_6H_4{\cdot}NO_2$-*p*).

(b) *From* trans-2-p-*nitrobenzamido*cyclo*pentanol* (I; R = $C_6H_4{\cdot}NO_2$-*p*). The nitrobenzamido-alcohol (12 g.) was dissolved in dry dioxan (20 ml.), 7N-solution (30 ml.) of hydrogen chloride in dioxan was added, and the mixture was heated in a sealed tube for 2 hours at 100°. The product (III; R = $C_6H_4{\cdot}NO_2$-*p*) (8·4 g.) had m. p. 189—191°. The mother-liquor was evaporated to dryness, and the residue treated with warm water (30 ml.). The insoluble portion (1·52 g.; m. p. 206—210°) appeared to consist mainly of 2-*hydroxy*cyclo*pentylammonium* p-*nitrobenzoate* (Found: N, 9·2. $C_{12}H_{16}O_5N_2,H_2O$ requires N, 9·7%) as, when its alkaline solution was acidified, *p*-nitrobenzoic acid was produced. The aqueous extract gave *cis*-2-*p*-nitrobenzamido*cyclo*pentanol (II; R = $C_6H_4{\cdot}NO_2$-*p*) (1·7 g.), m. p. 164—166° when it was made alkaline.

Acyl-migration Experiments with the Diastereoisomers (I) *and* (II); *General Procedure.*—Each diastereoisomer was dissolved in dry dioxan containing a known quantity of hydrogen chloride, and experiments then carried out at 25°, and in sealed tubes immersed in a steam-bath. In the *p*-nitrobenzamido-series, when the reaction had ended the precipitate (III; R = $C_6H_4{\cdot}NO_2$-*p*) was filtered off, the mother-liquor evaporated to dryness, and the residue extracted with water. A further crop of the amino-ester hydrochloride was obtained by evaporation, in a vacuum, of this extract.

With the benzamido-compounds this method of isolation proved unsatisfactory owing to similarities of solubility; therefore, separation was effected by fractional crystallisation from benzene–light petroleum. The experimental details are recorded in the table. Details of acyl migrations involving change of configuration have been described above.

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Institute of Organic Chemistry,
The University, Szeged, Hungary. [*Received, June 11th*, 1951.]

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292. *Absorption Spectra of Substances containing the Carbon–Iodine Bond. Part II.**

By T. M. Dunn and T. Iredale.

The absorption spectra of iodobenzene, the iodonaphthalenes, and 2-iododiphenyl in the near ultra-violet are described. Under suitable experimental conditions a brief, diffuse band system has been found in the vapour of iodobenzene at room temperature, and at 90° K in its solution in frozen light petroleum. The *O–O* bands of iodobenzene in the two states have been indicated. Reasons for the disposition and intensities of the bands of the iodonaphthalenes and of 2-iododiphenyl have been advanced.

In Part I * Iredale, Durie, and Jarvie described the absorption spectra of some compounds containing the C–I bond, in particular iodobenzene and iodoacetic acid. In the vapour state there appeared to be for both these substances a continuum in the 2600-Å region, although it was implied that in the case of iodobenzene not all of the absorption in this region may have been embraced in this phenomenon. This paper describes some experiments carried out to discover if there is any band system, possibly not very strong, which may be obscured by the accompanying continuum.

There is reason to believe that the absorption spectrum of iodobenzene is complex because of the accidental magnitudes of molar extinction coefficients of two different

* Part I, *J.*, 1950, 1181.

absorption processes: (i) excitation of π electrons in the ring, analogous to benzene and other halogenobenzenes, (ii) excitation of a non-bonding electron on the iodine. It is difficult to believe, however, that both these processes will be concurrent if there is much conjugation of the iodine with the ring.

An unusual trend is observed when the maximum extinction coefficient ($\varepsilon = 665$) of iodobenzene is compared with the extinction coefficients of the other halogenobenzenes in the same region:

		PhF	PhCl	PhBr
$\varepsilon_{max.}$	(1)	1650	310	243
	(2)	1061	236	200

(1) Conrad–Billroth, *Z. physikal. Chem.*, 1934, *B*, **25**, 139.
(2) American Petroleum Institute Research Project 54, National Bureau of Standards.

There is a progressive decrease of ε with increasing atomic weight of the halogen towards $\varepsilon = 220$ of benzene itself. Since the alkyl iodides have maximum extinction coefficients in the 2600-Å region of the order 400—500 [methyl iodide, 380; ethyl iodide, 460; propyl iodide, 480 (Hillmer and Paersch, *Z. physikal. Chem.*, 1932, *A*, **161**, 46)], it appears likely that the continuum is caused by an alkyl iodide type of absorption superposed on the banded type of absorption characteristic of the other halogenobenzenes. From the trend of the extinction coefficients of these benzene derivatives, iodobenzene would be expected to have for its banded absorption a maximum extinction coefficient $\varepsilon \sim 220$, the same as for benzene itself. This added to the alkyl iodide $\varepsilon = 400$—500 would give a total ε for the two effects of *ca.* 600—700, which is of the order of the observed value, *i.e.*, 665. Some reason must be found for the exceptional behaviour of the iodine atom.

On Sklar's hypothesis (*J. Chem. Physics*, 1939, **7**, 984) that absorption intensity depends upon the extent of migration of electrons into or out of the benzene ring, it would seem that in iodobenzene there is negligible migration. When the halogens are bonded to a benzene ring, there are four non-bonding electrons, two $np\pi_x$ and two $np\pi_z$ (the two-fold axis of rotation being taken as the y axis, and the z axis in the usual sense), and in the case of fluorobenzene where these electrons are $2p\pi_x$ and $2p\pi_z$ we know that there is a strong mesomeric effect tending to cause migration of the π_z electrons into the benzene ring, while the inductive effect more than overcomes this tendency, resulting in the effective dipole moment being away from the ring. This mesomeric migration of charge has been demonstrated theoretically by Coulson and Longuet-Higgins (*Proc. Roy. Soc.*, 1947, *A*, **191**, 39) who showed that, molecular orbitals being used for conjugated systems such as fluorobenzene, the electron density of the electrons on the halogen atom, q_r, is such that $0 < q_r < z$. Thus their analysis shows that even though the halogen atom is more electronegative than the carbon atom, it is, in fact, only the magnitude of the electron drift and not its direction which depends upon the nature, *i.e.*, the electronegativity, of the atom, in this case a halogen. Baddeley (*J.*, 1950, 663), from a consideration of available data, suggested that there was a relation between the size of an atom and its mesomeric effect. We have here spectroscopic evidence to support the idea of decreasing mesomeric effect down the halogen series from the small fluorine to the large iodine atom.

The long-wave ultra-violet band of the alkyl halides, and in particular the 2600-Å band of the alkyl iodides [Herzberg and Scheibe's *A* band (*Trans. Faraday Soc.*, 1929, **25**, 716)] has been attributed by Mulliken (*Phys. Review*, 1936, **50**, 1017, 1028; 1937, **51**, 310; *J. Chem. Physics*, 1940, **8**, 234, 382) to the weak perpendicular type $N \longrightarrow Q$ transitions. Price (*ibid.*, 1936, **4**, 539) suggests that the continuum is due to a strong form of predissociation resulting from this transition, rather than that the upper state is a pure repulsion, giving the continuum observed in practice.

This scheme shows that the transition involved is essentially localised on the iodine atom, or at most, since the 6*s* orbital of iodine is very large, it may be localised in the vicinity of the C–I bond, and so has hardly any effect on the molecule as a whole. The same effect is shown in Herzberg and Scheibe's *B*, *C*, and *D* bands (*loc. cit.*) which Mulliken suggests are due to a 5 $p\pi$ non-bonding electron of the iodine excited to a 6 $d\pi$ level, the transition being once more localised on the iodine atom.

Predissociation causes the bond to split with the transfer of one bonding electron to the carbon atom, and the molecule breaks into two neutral parts, one an iodine atom and the other a radical.

Further evidence for the assumption of a purely localised C–I absorption in iodobenzene can be obtained from a consideration of McClure's data (*J. Chem. Physics*, 1949, **17**, 905) on the oscillator strengths of halogenbenzenes :

	PhF	PhCl	PhBr	PhI	PhH
f	0·00816	0·00284	0·00249	0·0134	0·00147

These values have a fair error due to the difficulty of obtaining the correct summation when the bands have much structure, as in the case of all but iodobenzene. Mulliken's approximation (*J. Chem. Physics*, 1939, **7**, 14) $f = 4{\cdot}31 \times 10^{-9} \times \varepsilon_{max.} \times \Delta\nu$ being used, where $\Delta\nu$ is the " half band width " (this in the case of the alkyl iodides is about 5000 cm.$^{-1}$), $\varepsilon_{max.}$ has previously been seen to be about 450, and using these values we obtain the electron oscillator strength of the alkyl iodide continuum as 0·0097. This value when added to that for benzene gives an f for the combined alkyl iodide and benzene transitions equal to 0·0112, which is still somewhat removed from the experimental value of 0·0134. We have assumed that the extinction coefficient of the iodobenzene band absorption is about the same as for benzene itself; but it is probably greater than that, so the actual combined f value will be definitely greater than 0·0112.

Recently, Robertson and Matsen (*J. Amer. Chem. Soc.*, 1950, **72**, 5252) calculated the position and intensity of the halogenobenzene bands by the crude molecular-orbital theory in which allowance has been made for the inductive effect. Their order is $C_6H_5F > C_6H_5Cl > C_6H_5Br$ for the oscillator strengths. Iodobenzene was not considered because of the assumed diffuseness of the absorption. We have seen that iodobenzene falls into line with the other halogenobenzenes if the banded absorption be considered separately from the continuum.

Iodobenzene.—Hitherto we have only observed an absorption continuum, using the strong source of ultra-violet light, a modified form of the Allen hydrogen arc (Dunn, Durie, and Iredale, *Australian J. Sci.*, 1950, **12**, 143), and long exposures with the Hilger 3-metre grating spectrograph. There is some decomposition of the iodobenzene, and a film tends to form on the front window of the absorption cell, in spite of every precaution to prevent this. Possibly this is not the only explanation of the difficulty involved in obtaining discrete absorption bands of the kind found with the other halogenobenzenes. We next tried the absorption in a tube 150 cm. long with the vapour coming from an attached reservoir of the pure liquid kept at temperatures from −10° to room temperature (18°). The source of ultra-violet light was a hydrogen discharge tube of low intensity, of the type 2230 supplied with the Beckman DU spectrophotometer. The spectrograph was the Hilger medium quartz instrument. We also investigated the absorption of a light petroleum solution of iodobenzene, frozen to a solid glass at 90° K in a special apparatus to be described later. In this way we have obtained some diffuse bands, both in the vapour and in the frozen solution. They are degraded to the red. Their wave-lengths, wave-numbers, and separations from the band of longest wave-length are given in the following table :

Iodobenzene bands.

Vapour			Solid		
λ (Å)	ν(cm.$^{-1}$)	$\Delta\nu$	λ (Å)	ν(cm.$^{-1}$)	$\Delta\nu$
2502	39 970 m	3210	2576	38 820 s	2490
2547	39 260 s	2500	2643	37 840 s	1510
2613	38 270 s	1510	2679	37 330 w	1000
2683	37 270 m	510	2714	36 840 m	510
2721	36 760 w	—	2752	36 330 m	—

(s = strong; m = medium; w = weak.)

In benzene it is found that the ε_g^+ vibration has the value 520 cm.$^{-1}$ in the excited state, 606 cm.$^{-1}$ in the ground state. In the halogenobenzenes, this ground state vibration splits

into two : ~600 cm.$^{-1}$ of symmetry β_1, and a totally symmetric vibration of lower frequency, α_1 (Sponer, Nordheim, Sklar, and Teller, *J. Chem. Physics*, 1939, **7**, 207) :

	Ground state vibration		Excited state vibration		Ground state vibration		Excited state vibration
	β_1	α_1	β_1		β_1	α_1	β_1
PhF	617	520	517	PhBr	616	317	—
PhCl	615	418	521	PhI	614	268	510

Support for the assignment of 617 and 615 cm.$^{-1}$ in fluoro- and chloro-benzene is given by Wollman (*ibid.*, 1946, **14**, 123) from a comparison with the corresponding bands in benzene, and from a study of the Raman lines (Wittek, *Sitz. Akad. Wiss. Wien*, 1941, 2*B*, **150**, 1; Kohlrausch and Wittek, *ibid.*, p. 75).

The band at 2752 Å (36 330 cm.$^{-1}$) is assumed to be the *O–O* band. The *O–O* band in the vapour, assumed to be 2721 Å (36 760 cm.$^{-1}$), implies a red shift in the solid phase of 430 cm.$^{-1}$. From studies of fluoro- and chloro-benzene, Wollman (*loc. cit.*) concludes that the transition 0—2,β_1 can take place, and that this transition increases in intensity relatively to the 0—1 band intensity as the substituent changes from bromine to chlorine

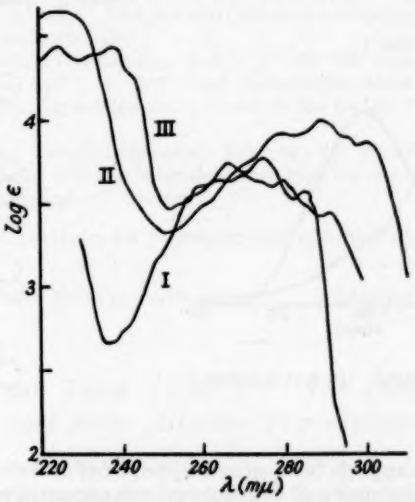


FIG. 1.

(I) *Naphthalene.*
(II) α-*Iodonaphthalene.*
(III) β-*Iodonaphthalene.*
(*All in* n-*heptane.*)

to fluorine. This illustrates the increasing importance of the vibration mechanism in allowing the electronic transition in the order F > Cl > Br > I, and explains the very weak band at 2679 Å ($\Delta\nu$ = 1000 cm.$^{-1}$), in the iodobenzene spectrum in the solid phase, which has no counterpart in the vapour.

The red shift of the *O–O* band of iodobenzene vapour relatively to benzene is then 1330 cm.$^{-1}$ compared with 1093 and 1037 cm.$^{-1}$ for bromo- and chloro-benzene.

We are unable to confirm Sreeramurty and Rao's finding (*Curr. Sci.*, 1949, **18**, 418) of about 100 bands of iodobenzene in the 2400—2800-Å region. As they gave no experimental details, we are unable to compare their results with ours. We hope to improve experimental conditions and discover more bands, which are doubtless obscured by the continuum.

Iodonaphthalenes.—As α- and β-iodonaphthalene have very low vapour pressures at room temperatures, special heating arrangements must be adopted to obtain a reasonable vapour pressure and quantity of absorbing gas in an absorption tube of convenient length. We have worked up to temperatures of 75°, when absorption becomes appreciable. One or two bands have appeared, but the crowding together of so many bands, caused by the greater number of transitions allowed in the naphthalene structure as compared with benzene, and the operation of the Boltzmann factor at the higher temperatures, makes

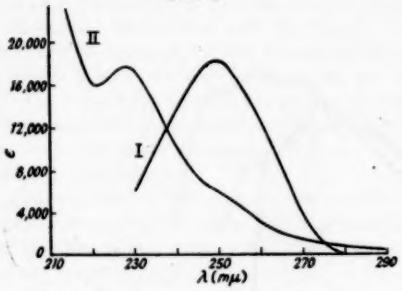
their identification almost impossible. We hope to obtain more satisfactory results with long absorption tubes at lower temperatures.

In heptane solution a banded structure is obtained both for the α- and the β-compound, and the relation of this absorption to that of naphthalene is shown in Fig. 1. The molar extinction coefficients (ε) in the 2600-Å region are of the order 4×10^3, so that the π electron absorption in this case completely swamps the aliphatic C–I ($N \longrightarrow Q$ transition) absorption, where $\varepsilon \sim 600$.

Of the two absorption bands, the long-wave band of naphthalene may be considered to be due to a transverse polarization through the 1- and 4-positions, and the short-wave band to a longitudinal polarization. In the case of α-iodonaphthalene, the long-wave band has increased in intensity and shifted to the red, whereas for the β-compound, the short-wave band has shifted toward the red, and the long-wave band is almost in the same position as in naphthalene.

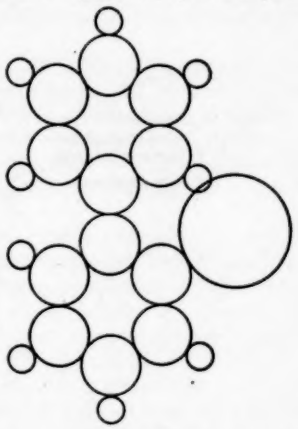
2-Iododiphenyl.—The absorption spectrum of this compound requires special explanation, since it does not follow regularly the expected change upon substitution of iodine in the diphenyl nucleus. The maximum appears to have been shifted to the short-

FIG. 2.



(I) *Diphenyl.*
(II) *2-Iododiphenyl.* (*Both in* n-*hexane.*)

FIG. 3. *Planar configuration of 2-iododiphenyl.*



wave side, and there appears to be an overlapped band in the region of 2500 Å (Fig. 2). (The absorption of both diphenyl and iododiphenyl was measured with the Beckman instrument.) Steric effects are of importance in this case. O'Shaughnessy and Rodebush (*J. Amer. Chem. Soc.*, 1940, **62**, 2906) have discussed the cases of 2 : 2'-disubstituted diphenyls, but here we have a case where steric hindrance occurs without a second substituent group. Reference to a scale drawing of the molecule (Fig. 3 : diameter of small circle = 0·62 Å) shows that, even when the effect of bond shortening is neglected, there is considerable overlapping of the hydrogen and iodine orbitals. This undoubtedly leads to a twisting of the molecule out of the planar configuration, resulting in a loss of delocalization energy of the π electron systems. This will lead to a breakdown of the long-wave band of diphenyl, owing to the destruction of the diphenyl symmetry. The spectrum will tend to revert to a composite spectrum of the two mutually unconjugated parts of the molecule. This effect will not be complete, owing to the fact that the angle of twist would not be a complete right angle. This explains the appearance of the band at about 2290 Å, but does not account for the apparently overlapped band. It is suggested that this band is also present in the spectrum of diphenyl, but it is hidden by the band of stronger transition in the same region. It is most likely connected with absorption of light with the electric vector perpendicular to the two-fold axis in diphenyl, and is uncovered when the stronger transition is displaced to shorter wave-lengths, as well as being slightly displaced to the red itself, owing to substitution by iodine in the *o*-position. Platt (*J. Chem. Physics*, 1951,

19, 101) predicted from a study of the energy levels of molecules iso-π-electronic with diphenyl, such as fluorene, that such a hidden transition should exist. Now Pestemer and Meyer-Pitsch's study of substituted diphenyls (*Monatsh.*, 1937, **70**, 104) also supports this prediction. Their absorption curves for *p*-substituted diphenyls show no trace of a long-wave step, whereas the curves for *m*- and *o*-substituted compounds show such overlapped transitions clearly. The *m*-substitution obviously shifts the transversely polarized band to the red, and leaves the main band almost stationary. In *p*-substituted compounds the strong band still overlaps the band of weaker transition, but in *o*-compounds both steric hindrance and the red shift of the weaker transition cause it to be uncovered.

On account of the high extinction coefficients of these allowed transitions ($\varepsilon > 10^4$), all evidence of a localized, C–I aliphatic absorption has vanished, nor may we expect to find it again, except in compounds like iodobenzene which have an absorption due to a transition of low probability, in the 2600-Å region.

Experimental.—Details of the optical apparatus and methods of measuring the absorptions are given in Part I (*loc. cit.*).

Hexane and heptane were purified by repeated shaking with fuming sulphuric acid, washing, drying, and distilling. They transmitted satisfactorily down to 2200 Å. Light petroleum (b. p. 60—80°) was purified in the same way. The material set to a transparent, glassy solid when quickly frozen with the aid of liquid nitrogen.

Iodobenzene, purified by vacuum distillation, had b. p. 189°/760 mm., α-iodonaphthalene, purified by vacuum distillation, had b. p. 302°, and β-iodonaphthalene, purified by steam-distillation followed by three vacuum sublimations, in which the middle fraction was retained, melted at 53°.

2-Iododiphenyl, purified by steam-distillation, followed by vacuum distillation, had b. p. 110°/0·5 mm. We considered that the substance examined was sufficiently pure when its spectral characteristics did not change any further.

We are indebted to Mr. J. Ferguson for photographing and identifying the iodobenzene bands.

PHYSICOCHEMICAL LABORATORIES, UNIVERSITY OF SYDNEY. [*Received, October 29th*, 1951.]

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293. *Picrotoxin and Tutin. Part V.* The Dehydration of Picrotin and Some Alkaline Degradations.*

By S. N. SLATER and A. T. WILSON.

(With an Appendix by M. SUTTER and E. SCHLITTLER.)

Dehydration of picrotin with oxalic acid gives a mixture which on bromination yields bromo*neo*picrotoxinin and a second bromo-derivative not identical with any known bromopicrotoxinin. Degradation of dihydro-*neo*picrotoxinin with hot sodium carbonate solution gives δ-hydroxy-γ-keto-β-*iso*propylvaleric (I) and 5-hydroxy-3-keto-2-methyl*cyclo*pent-1-ene-1-carboxylic acid (II), whereas picrotin under the same conditions yields the *cyclo*pentene acid and an acid which may be δ-hydroxy-β-(1-hydroxy-1-methylethyl)-γ-ketovaleric acid (III). A convenient method of separating (I) and (II) is described. An appendix gives details of the oxidation of dihydropicrotoxinin to *iso*butyric acid and of picrotin to α-hydroxy*iso*butyric acid.

IN Parts III and IV (*J.*, 1949, 806; 1952, 185) we discussed the functional groups of picrotin and picrotoxinin. We now record experiments designed to elucidate the relation between the two substances. It has long been suspected that this must be close, for, *e.g.*, each can be converted into picrotic acid (Angelico, *Gazzetta*, 1911, **41**, ii, 337), the chloro-ketone $C_{14}H_{15}O_3Cl$ (*idem, Atti R. Accad. Lincei*, 1910, [v], **19**, i, 473), and picrotonol (*idem, Gazzetta*, 1910, **40**, i, 391; O'Donnell, Robertson, and Harland, *J.*, 1939, 1261;

* Part IV, *J.*, 1952, 185.

Slater, *J.*, 1949, 806). The simplest assumption would be that picrotin, $C_{15}H_{18}O_7$, is related to the olefin picrotoxinin, $C_{15}H_{16}O_6$, by simple addition of water :

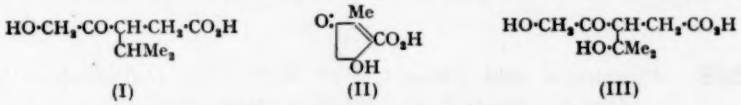
Picrotoxinin, $C_{12}H_{11}O_6 \cdot C(:CH_2) \cdot CH_3$ Picrotin, $C_{12}H_{11}O_6 \cdot C(CH_3)_2 \cdot OH$

and Schlittler and Sutter (Sect. 6, 1st Int. Congr. Biochemistry, Cambridge, 1949) reported that, in agreement with this, oxidation of dihydropicrotoxinin with alkaline permanganate yields *iso*butyric acid whereas picrotin yields α-hydroxy*iso*butyric acid. Nevertheless no direct interconversion has yet been recorded, the nearest approach being the dehydration of α-picrotinic acid by heat to picrotoxic acid (Horrmann, *Annalen*, 1916, **411**, 273) :

$$\begin{array}{ccc} \text{Picrotin, } C_{15}H_{18}O_7 & \xrightarrow[\text{acid}]{\text{Mineral}} & \text{α-Picrotinic acid, } C_{15}H_{20}O_8 \\ & & \downarrow -H_2O \\ \text{Picrotoxinin, } C_{15}H_{16}O_6 & \xrightarrow[\text{acid}]{\text{Mineral}} & \text{Picrotoxic acid, } C_{15}H_{18}O_7 \end{array}$$

However, since both picrotin and dihydropicrotoxinin are complex substances readily degraded by alkali, the products of oxidation under alkaline conditions can give little information about the molecule as a whole (the Swiss authors apparently recognise the existence of as yet undefined differences between picrotin and picrotoxinin). In any case, until the relations of α-picrotinic acid to picrotin, and of picrotoxic acid to picrotoxinin, are determined, there is no direct evidence for the above simple olefin–hydrate relation.

A further link between the two series has now been found in the degradation of picrotin to the acid (II) previously isolated from the products of alkaline degradation of picrotoxinin, dihydropicrotoxinin, α-picrotoxinic acid, and dihydro-α-picrotoxinic acid (Sutter and Schlittler, *Helv. Chim. Acta*, 1949, **32**, 1855, 1864; 1950, **33**, 902). When a picrotin solution containing sodium hydrogen carbonate is concentrated by boiling, it rapidly becomes brown and no picrotin is recovered. When heated with carbonate solution, picrotoxinin behaves similarly. This suggested that fission of the picrotin molecule might be taking place and further investigation confirmed this. With the hope that this method might be valuable if applied to tutin we first adapted Sutter and Schlittler's methods



(I) (II) (III)

to the working-up of small quantities of degradation products. Since (II) is a stronger acid than (I), the accompanying degradation product of dihydropicrotoxinin, and the carbonate degradation solution acts as a buffer, acidification to pH *ca.* 6 leaves (II) almost completely as its anion while (I) is almost completely un-ionised and is readily removed by continuous extraction with ether. Further acidification and ether-extraction of the solution then removes (II). The constants of the two acids agreed with those recorded by Sutter and Schlittler, except that in the spectrum of (I) we found $\lambda_{max.}$ 279 mμ whereas the Swiss workers give 260 mμ. Professor Schlittler has since advised us that the latter figure should have read $\lambda_{max.}$ 276 mμ. Alternatively (I) and (II) were separated by using an ion-exchange column.

The alkaline degradation of picrotin was then attempted and yielded finally (II) and a more weakly acidic fraction which proved extremely difficult to manipulate, largely owing to its tendency to revert to an oily lactone. Neither the free acid nor the lactone could be obtained pure. The properties, and the lack of carbonyl activity, are very similar to those of (I) and are not incompatible with the structure (III) which is that of the product of alkaline degradation to be expected if the carbon skeletons of picrotin and picrotoxinin are identical. Further, we have found that dihydro*neo*picrotoxinin is degraded in hot carbonate solution to (I) and (II), and this taken in conjunction with the dehydration of picrotin to *neo*picrotoxinin (see below) and the evidence cited at the beginning of this paper provides support for this view.

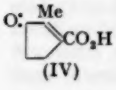
In the light of the above results the failure of previous workers to dehydrate picrotin

to a " picrotoxinin " appeared to us most unexpected unless that hydroxyl group which appears in α-hydroxybutyric acid and (III)—both isolated from *alkaline* reaction mixtures—is bound by lactone formation in picrotin itself. We therefore tried to dehydrate the sodium salt of the " true picrotinic acid " (the as yet unisolated hydroxy-acid formed as the salt when picrotin is dissolved in cold, dilute, aqueous sodium hydroxide). When the dry sodium salt was fused with oxalic acid and the product brominated, a small amount of bromo*neo*picrotoxinin was isolated (Slater and Wilson, *Nature*, 1951, **167**, 324). When picrotin itself was fused with oxalic acid and brominated, it yielded, somewhat unexpectedly, a mixture of bromo*neo*picrotoxinin and another bromo-derivative; yields were very small and variable and it has not been possible to obtain sufficient of this new material for a full investigation. It is similar to the known bromopicrotoxinins (α-, β-, and *neo*-) in giving with alkali an acid somewhat similar to α- and β-bromopicrotoxinic acids, but shown by crystallographic examination to be different from either. (We are indebted to Mr. J. J. Reed, Petrologist to the Geological Survey of the New Zealand Department of Scientific and Industrial Research, for this and other optical examinations.) We suggest tentatively that the new bromo-derivative and the corresponding acid are derived from an isomer of *neo*-picrotoxinin, formed by the alternative dehydration of picrotin to give the *iso*propenyl rather than the *iso*propylidene system:

$$\text{Picrotin, } C_{15}H_{11}O_6\cdot CMe_2\cdot OH \xrightarrow{-H_2O} \begin{cases} \rightarrow C_{15}H_{10}O_6{:}CMe_2, \textit{neo}\text{Picrotoxinin} \\ \rightarrow C_{15}H_{11}O_6\cdot CMe{:}CH_2\ ? \end{cases}$$

It appears, therefore, that picrotin is related to *neo*picrotoxinin rather than to picrotoxinin. This may be correlated with previous observations that picrotin and *neo*picrotoxinin can be acetylated, whereas picrotoxinin cannot (under comparable conditions), and that picrotin and *neo*picrotoxinin with hot dilute mineral acid yield picrotonol whereas picrotoxinin yields picrotoxic acid.

Sutter and Schlittler obtained succinic acid on permanganate oxidation of picrotin, picrotin acetate, or picrotoxinin; if this is formed directly, it indicates the existence of the fragment $\cdot CH_2\cdot CH_2\cdot$ in these substances. The oxidations, however, were carried out after the compounds had been heated at *ca.* 90° with sodium carbonate solution, which would presumably cause extensive degradation to (II), etc.; the oxidation products isolated might then be largely derived from these artefacts. Although (II), the common product isolated from all alkaline degradation mixtures so far investigated, does not admit of oxidation to succinic acid, its deoxy-derivative (IV) has been obtained in (relatively) high yield by degradation of picrotoxinin with hot barium hydroxide solution (Sutter and Schlittler, *loc. cit.*, 1949), and the succinic acid may have arisen from this source. No succinic acid was isolated on oxidation of dihydropicrotoxinin; in this experiment the preliminary heating with carbonate solution was to 20° only and the isolation of dihydropicrotoxic acid from the oxidation reaction shows that degradation had not proceeded so far as in the other cases.



(IV)

Experimental

Alkaline Degradation of Dihydropicrotoxinin.—Finely powdered dihydropicrotoxinin (5 g.) was dissolved in 10% sodium carbonate solution (730 ml.) at 80° while being agitated with a stream of nitrogen (30 minutes). The mixture, after continuous ether-extraction for 24 hours, was acidified with concentrated hydrochloric acid to pH *ca.* 6 and extracted with ether for 14 hours (extract A). Further 6-hour extractions were made until no more material was removed (extracts B). The aqueous layer was then acidified to Congo-red and extracted for 12 hours (extract C). Extract A was dried (Na_2SO_4), evaporated, and kept overnight in the refrigerator. A semicrystalline product was obtained from which resinous material was removed with a little ether, leaving white crystals (500 mg.) of δ-hydroxy-γ-keto-β-*iso*propylvaleric acid (I). A further quantity (200 mg.) was obtained by working up the ethereal mother-liquor. Recrystallised from ether–light petroleum (b. p. 40—60°), it had m. p. 110—110·5° (Found: C, 54·8; H, 7·9. Calc. for $C_8H_{14}O_4$: C, 55·2; H, 8·1%), $\lambda_{max.}$ 279 mμ (log ε = 1·56). Extracts B yielded oils which were not further investigated, although no doubt they contained

much of the lactone of the acid. Extract C, worked up in the same way as extract A, gave 5-hydroxy-3-keto-2-methyl*cyclo*pent-1-ene-1-carboxylic acid (210 mg.), crystallising from ether in bundles of small needles, m. p. 156° (Found: C, 53·5; H, 5·1. Calc. for $C_7H_8O_4$: C, 53·8; H, 5·2%), $\lambda_{max.}$ 234 (log ε = 4·02) and 332 mμ (log ε = 1·57).

Separation of Acids (I) *and* (II) *by Ion-exchange.*—A mixture of (I) (*ca.* 150 mg.) and (II) (*ca.* 140 mg.) in water (20 ml.) was passed down a column of " De-Acidite B " (20 × 1/2"), being followed by water. The first 20 ml. were returned to the top of the column and 90 ml. then collected and ether-extracted, to yield (I) (130 mg.). After the column had been washed with a further quantity of water (150 ml.), 10% sodium carbonate solution was passed through and 90 ml. were collected and worked up, to yield (II) (110 mg.).

Dihydroneopicrotoxinin.—Picrotoxin (6 g.) in alcohol was hydrogenated in the presence of palladium chloride (0·3 g.) dissolved in dilute hydrochloric acid (from 6 drops of concentrated acid) until no more hydrogen was absorbed (48 hours). Alcohol was removed and the product heated under reflux with 3% sulphuric acid (300 ml.) for 18 hours. Large plate-like crystals (0·57 g.) separated from the cold solution, and a further quantity (0·91 g.) was obtained by addition of an excess of sodium hydrogen carbonate and extraction with ethyl acetate. The product had m. p. 256° (from alcohol).

Alkaline Degradation of Dihydroneopicrotoxinin.—Finely ground dihydro*neo*picrotoxinin (1·5 g.) was heated with 10% sodium carbonate solution (80 ml.) at 90° with agitation by nitrogen. After 25 minutes the reaction mixture was cooled and ether-extracted for 24 hours (nothing was extracted). The reaction mixture was then made faintly acid to Congo-red; the yellow colour of the solution faded as did that of the solution obtained from dihydropicrotoxinin. The solution was again ether-extracted for 24 hours and on evaporation of the dried extract a light yellow oil remained. When seeded with the acid (I), this yielded crystalline (I) (21 mg.), m. p. 109°, mixed m. p. 110°. The aqueous solution was then acidified more strongly and again ether extracted for 24 hours, to yield finally a light yellow oil (105 mg.) which when seeded with the acid (II) deposited crystals, m. p. 152°, mixed m. p. with (II), 154°. The identities of the degradation products were confirmed by comparison of the absorption spectra.

Alkaline Degradation of Picrotin.—Finely powdered picrotin (5 g.) was heated with 10% sodium carbonate solution (730 ml.) at 70—75° with agitation by nitrogen. After 30 minutes the amber-coloured solution was steam-distilled (no acetone was detected), the colour changing to orange. The resulting solution was ether-extracted for 12 hours, to yield a little unchanged picrotin. Ether-extractions were then made at pH 6·5 (a little oil), pH 5 (a red oil, 1·89 g.) and pH 3 (some oil, finally yielding crystals of acid (II) (mixed m. p. and identical absorption spectra). The red oil was dissolved in ether and chromatographed on alumina. The ether was followed by ether containing 10% of methanol, ether containing 50% of methanol, and finally methanol. A little white solid material was isolated from the final methanolic elution, the other extracts yielding brown and (mainly) red oils. An attempt to crystallise the above-mentioned white solid from alcohol gave only a red oil, insoluble in ether. However, when dissolved in dilute sodium hydroxide solution and then acidified, it could again be extracted with ether. A crystalline specimen was not obtained, the acid forming the ether-insoluble lactone, even below 90°.

Dehydration of the Sodium Salt of the " True Picrotinic Acid."—Picrotin (2 g.), dissolved in 2% sodium hydroxide solution, was titrated with acid until only just alkaline and the water removed under reduced pressure from a water-bath at 30—40°. A white glassy solid remained, which could be ground to a powder but on exposure to the air rapidly became sticky. This was ground with fused oxalic acid (2 g.) and the mixture heated at 110° for 24 hours. The resulting brown cake was dissolved in boiling water and a brown supernatant oil removed (crude picrotin?). The solution was filtered and treated with bromine water. The white precipitate which formed coagulated into a few clots which were filtered off and crystallised from ethyl alcohol several times, to give needles, m. p. 264° alone or mixed with authentic bromo*neo*picrotoxinin of the same m. p. The yield was only 3—4 mg.

Dehydration of Picrotin.—On account of the small yield of bromo-derivative obtained in the dehydration experiments special care was taken to remove all traces of bromopicrotoxinin from the picrotin used. This is best done by dissolving the picrotin in cold dilute alkali and filtering off any insoluble material. Acidification regenerates very pure picrotin. Picrotin (1 g.) was added to oxalic acid (2 g.) melted in a test-tube. The resulting clear colourless solution was kept just at the f. p. for about 30 minutes, then cooled and dissolved in hot water. On addition of bromine water a white precipitate appeared which was filtered off, washed with dilute alkali to remove unchanged picrotin and oxalic acid, and then crystallised from ethyl

alcohol as small cubes, m. p. 264° (*ca.* 5 mg.). The alcoholic mother-liquors gave bromo*neo*-picrotoxinin.

The former substance (*ca.* 5 mg.) was suspended in hot water (0·5 ml.), and dilute aqueous sodium hydroxide added dropwise until dissolution was complete. The product was cooled and acidified carefully, yielding a white precipitate which, crystallised from water, had m. p. *ca.* 250°. This acid has α 1·532 ± 0·001, β = 1·558 ± 0·001, and γ = 1·562 ± 0·001, the measurements being made with sodium light. Petrographic examination of α-bromopicrotoxinic acid was hindered because of the fine needle-like crystals in which it separates, but the following measurements were made: α = 1·546 ± 0·002, γ = 1·549 ± 0·002. When samples of the new acid and α-bromopicrotoxinic acid were immersed in a liquid of n_D 1·5472, the lowest refractive index (α) of α-bromopicrotoxinic acid was considerably higher, whereas that of the unknown was less. The highest refractive index (γ) of β-bromopicrotoxinic acid exceeded 1·583.

Appendix

Oxidation of Picrotin with Potassium Permanganate in Cold Alkaline Solution.—Picrotin (10 g.) was dissolved by heating it for 15 minutes at 90° with 15% sodium carbonate solution (1 l.). The reddish-yellow solution was then cooled to 0° and potassium permanganate (19 g.) in ice-cold water (950 ml.) added slowly with stirring during 1 hour. The mixture was then set aside for 16 hours. The manganese dioxide was brought into solution with sulphur dioxide, and the whole concentrated to 200 ml. at 40°, acidified with concentrated sulphuric acid to Congo-red, and ether-extracted for 24 hours. The ethereal solution was evaporated and the residue dissolved in water (10 ml.) and made alkaline with ammonia. Addition of an ammoniacal solution of calcium chloride precipitated oxalic acid as the calcium salt, which was filtered off, and the filtrate was again acidified and ether-extracted for 30 hours. The ethereal extract was dried (Na_2SO_4), evaporated, and then sublimed, with the following results: bath 100°/12 mm., sublimation temp. 60—80°, α-hydroxy*iso*butyric acid, m. p. 78—80° (0·332 g.); bath 120—160°/12 mm., succinic acid, m. p. 178·5—180°.

It is known that *iso*butyric acid itself can be oxidised by potassium permanganate to the α-hydroxy-acid. Experiments showed that this is possible only when the oxidation is carried out with heating. At 0° α-hydroxy*iso*butyric acid was not isolated.

Oxidation of Picrotin Acetate with Potassium Permanganate in Cold Alkaline Solution.—Picrotin acetate (4 g.) and 15% sodium carbonate solution (400 ml.) were heated for 15 minutes on the water-bath. The resulting solution was then oxidised at 0° with potassium permanganate (12·5 g.) in water (500 ml.). When worked up as above, the product yielded succinic acid but no α-hydroxy*iso*butyric acid.

Oxidation of Picrotoxinin with Potassium Permanganate in Cold Alkaline Solution.—Picrotoxinin (5 g.) was dissolved in 1% sodium carbonate solution (500 ml.) at 90° (5 minutes) (no acetone formed) and then cooled to 0°. Potassium permanganate (16·25 g.) in ice-cold water (650 ml.) was added with stirring. The mixture was clarified with sulphur dioxide, made slightly alkaline, concentrated *in vacuo* to 100 ml., and continuously extracted with ether (no residue on evaporation). The aqueous solution was then acidified with sulphuric acid to Congo-red and ether-extracted for 48 hours. The ether on evaporation left a syrupy residue containing oxalic acid, which was removed as the calcium salt (cf. above). The resulting ammoniacal solution was acidified and ether-extracted and the syrup remaining after evaporation of the ether sublimed at 120—130° (bath)/0·1 mm. The solid sublimate was transformed into the calcium salt, and again traces of the sparingly soluble oxalate separated. The syrup, which was now free from oxalic acid, was treated with acetone, pure succinic acid being obtained (0·27 g.), with m. p. 181—182° (phenylhydrazine salt, m. p. 95—96°).

Oxidation of Dihydropicrotoxinin with Potassium Permanganate in Alkaline Solution at 50°.—Dihydropicrotoxinin (2 × 5 g.) was dissolved in 1% sodium carbonate solution (2 × 1 l.) at 20°. Powdered potassium permanganate (2 × 22 g.) was then added and the solutions were heated to 55° for 19 hours with stirring. The vessel was connected to a trap cooled to −80°. The mixture was clarified with sulphur dioxide and made strongly alkaline and distilled in steam for a short time. Acetaldehyde was isolated as the 2 : 4-dinitrophenylhydrazone, m. p. 156—158° (Found: C, 43·1; H, 3·5; N, 24·5. Calc. for $C_8H_8O_4N_4$: C, 42·9; H, 3·6; N, 25·0%) (yield, as aldehyde, 0·12 g.). The steam-distilled alkaline solution was concentrated *in vacuo* to 500 ml. and extracted with ether. This extract left no residue. The aqueous solution was acidified with sulphuric acid (cooling) to Congo-red and ether-extracted for 3 days. The oil remaining after evaporation of the ether yielded, as above, 3·39 g. of pure oxalic acid. The

ammoniacal solution was acidified with sulphuric acid to Congo-red and extracted with ether. The extract yielded dihydropicrotoxic acid (0·95 g.), m. p. 253—254° (Found: C, 57·8; H, 6·4. Calc. for $C_{15}H_{20}O_7$: C, 57·7; H, 6·4%), and a viscous reddish-yellow oil. This oil gave the following fractions at 12 mm.: b. p. 53—54°, converted into *p*-phenylphenacyl *iso*butyrate, m. p. 84·5—85·5° (yield, as acid, 65 mg.); b. p. 88—90° (no crystalline *p*-phenylphenacyl ester); b. p. 108—110° (*p*-phenylphenacyl ester, m. p. 108—140°); b. p. 128—129° (no crystalline *p*-phenylphenacyl ester); and b. p. from 130°, a red-brown glassy mass, which after esterification (diazomethane) gave on distillation at 12 mm. fractions of b. p. 78—80°, 90—104°, and 125—128° respectively.

Acetaldehyde and *iso*butyric acid were also isolated when dihydro-α-picrotoxinic acid was oxidised with potassium permanganate.

One of us (A. T. W.) acknowledges the tenure of a Public Service Commission Bursary while on leave of absence from the Department of Scientific and Industrial Research. We thank the Director of the Dominion Laboratory for the use of certain facilities, Dr. T. S. Ma of the Microchemical Laboratory of the Chemistry Department, the University of Otago, under whose supervision the microanalyses recorded in the main body of the Experimental section were carried out, and particularly Professor Schlittler and Dr. Sutter for making available the results of unpublished experimental work recorded in the Appendix. The work has been facilitated by a grant from the Research Fund of the University of New Zealand.

VICTORIA UNIVERSITY COLLEGE,
WELLINGTON, NEW ZEALAND.

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294. *Some Observations concerning the Interpretation of Heats of Hydrogenation of Olefinic Substances.*

By P. B. D. DE LA MARE.

The theoretical implications of a recent analysis of tautomeric equilibria governed by the hyperconjugative power of alkyl groups on the one hand, and the conjugative power of phenyl, carboxylate ion, carbethoxy-, and cyano-groups on the other, as well as of the heats of hydrogenation of substituted ethylenes (*J.*, 1951, 2283), are scrutinised. The same experimental results are treated to an equally good approximation, empirical data rather than theoretically deduced resonance energies being used as far as possible. It is concluded that alkyl groups probably affect heats of hydrogenation of substituted ethylenes by their inductive, as well as by their hyperconjugative, effect.

BATEMAN and CUNNEEN (*J.*, 1951, 2283) have presented experimental data on the substituted phenylpropenes, in which the position of prototropic equilibrium is governed by the relative energies of conjugation, with an ethylenic double bond, of a phenyl group on the one hand, and of one or more alkyl groups on the other. The influence of different alkyl groups is regarded by these authors as correlated with (*a*) the extent of C–H bond first-order hyperconjugation and (*b*) the operation of a specific effect on replacement of a CH_2 group by CHR. These values, together with a selection of heats of hydrogenation of substituted ethylenes (from the work of Kistiakowsky and his co-workers, *J. Amer. Chem. Soc.*, 1935, **57**, 65, 876; 1936, **58**, 137, 146; 1938, **60**, 440), and values for the positions of equilibrium in systems involving αβ- and βγ-unsaturated acids, esters, and nitriles (from the data of Linstead, Kon, and their collaborators, summarised in Gilman's "Organic Chemistry," Wiley and Sons, N.Y., 2nd edn., 1944, p. 1042), are analysed in terms of a number of postulates (Treatment 1), namely:

(1*a*) That energy differences determined from the heats of hydrogenation (ΔH) of ethylene (32·6 kcal.) and substituted ethylenes may be used to calculate resonance energies, *e.g.*, of benzene (39 kcal.), butadiene (5·1 kcal.), and phenyl-to-vinyl conjugation (2·6 or 3·4 kcal.), which operate additively, and may be applied to the calculation of free-energy differences in prototropic systems.

(1*b*) That the energies of conjugation between an ethylenic link and a carboxylate ion, carbethoxy-, and cyano-group are respectively 1·5, 2·0, and 2·0 kcal.

(1*c*) That the hyperconjugative energy (i) of each single C–H bond with an ethylenic, butadienoid, or phenyl system is 0·3 kcal., (ii) of a C–H bond with a carboxylate ion, carbethoxy-, or cyano-group, is 0·2 kcal., (iii) of a C–C bond with an ethylenic system is negligible except in the absence of C–H bonds, and then is 0·03 kcal. per C–C bond.

(1*d*) That substitution at a CH_2 group in ethylene, irrespective of its nature, introduces a stabilising factor (*S*), which reduces the heat of hydrogenation by 1·5 kcal., while further substitution, whether by one, two, or three groups, introduces a further stabilisation of 1·5 kcal.

The Appendix shows the observed and calculated values. The fit is better for heats of hydrogenation and prototropic equilibria in the substituted phenylpropenes than for the remainder of the data.

In the author's view, this analysis suffers from at least one important unsatisfactory feature, namely, the introduction and the interpretation of the structural factor *S*, on which special emphasis is laid. It is stated that its origin is uncertain, but that it may arise from some interaction between the π-electrons of the methine carbon atom and the sp^3 orbitals of an adjacent saturated carbon atom. Yet this is not considered to be a form of hyperconjugation (not even CC-hyperconjugation), since CC- and CH-hyperconjugative effects are considered separately, and since *S* is held to be largely responsible for certain effects previously attributable to hyperconjugation. It appears to be regarded as related to the strength of the single bond in the system C=C–C; consistently, it is doubled in dialkylethylenes, whether these are 1 : 1- or 1 : 2-substituted; but, inconsistently, further substitution to give tri- or tetra-substituted olefins is regarded as contributing no further to the stabilisation of the molecule.

These difficulties suggest a reconsideration of the data, and it is submitted that the following postulates (Treatment 2) give an equally good account of the determined values:

(2*a*) That energy differences determined from the heats of hydrogenation of ethylene 312·6 kcal.), benzene (49·8 kcal.), butadiene (57·1 kcal.), and styrene (77·5 kcal.) may be applied to the correlation of heats of hydrogenation and free-energy differences in prototropic systems, with the following additional postulates.

(2*b*) That the system $CH_2{:}CH{\cdot}CH_2X \rightleftharpoons CH_3{\cdot}CH{:}CHX$, where X is CO_2^-, CO_2Et, or CN, lies to the right by virtue of a free-energy difference of 2·5 kcal.

(2*c*) That substitution for hydrogen of any alkyl or substituted-alkyl group reduces the heat of hydrogenation of (i) an ethylenic or butadienoid system by 2·3 kcal., (ii) a benzene nucleus by 0·9 kcal., (iii) the system $CH_2{:}CHX$, where $X = CO_2^-$, CO_2Et, or CN, by 1·0 kcal.

(2*d*) That the effectiveness of any alkyl group in the above situations is reduced by 0·5 kcal. for each cross- or opposed-hyperconjugation involving another alkyl group or a butadiene system.

The Appendix shows that Treatment 2 gives an account of the data which is at least as good as that of Treatment 1; it involves adoption of fewer particular numerical values, and is considered preferable as it uses fewer hypotheses. Let us now consider its theoretical implications.

In hypotheses (2*a*) and (2*b*) the argument depends on actual experimental figures, rather than on the derived resonance energies, used in the corresponding postulates (1*a*) and (1*b*) of Treatment 1. The value for the resonance energy of benzene obtained from these data is likely to be inexact; for although the heat of hydrogenation, *e.g.*, of *cyclo*hexene (28·6 kcal.) is similar to that of other 1 : 2-dialkylethylenes, the corresponding values for *cyclo*pentene (26·9 kcal.), *cyclo*heptene (26·5 kcal.), and particularly *cyclo*octene (23·5 kcal.) show discrepancies which are not properly understood (cf. Wheland, "Theory of Resonance," John Wiley and Sons, N.Y., 1944, p. 54; Dewar, *Trans. Faraday Soc.*, 1946, **42**, 767). It seems, therefore, that the properties of ethylenic links, when these are included in rigid or distorted ring structures, may be altered by factors other than those generally included in the category of resonance. Deductions in a conventional way of the resonance energies of butadiene conjugation (8·1 kcal.) and of phenyl-to-vinyl conjugation (4·0 kcal.) are larger in the present than in the earlier treatment, since in the latter the

structural factor S is introduced (unnecessarily, in our view) into the calculations. It is preferred not to attempt to differentiate between the relative conjugative power with a double bond of the groups CO_2^-, CO_2Et, and CN (which may be calculated, on the present assumptions, to be worth 3·8 kcal. in stability), since it is considered that the data on the relevant systems are not sufficiently self-consistent to allow such differentiation. The present preference in regard to these first two assumptions is not, however, regarded as fundamental, but rather as a matter of formal convenience.

Hypothesis (2*c*) reveals the first major divergence between the two treatments. In Treatment 1 it is assumed that, in conjugation with the double link, each C–H bond has a hyperconjugative effect, which is some ten times greater than that of a C–C bond, and contributes 0·3 kcal. to the stability. In the present treatment, it is taken that the attachment of any tetrahedral carbon atom to the ethylene system has approximately the same effect on the heat of hydrogenation. The following comparisons from the work of Kistiakowsky and his co-workers (*locc. cit.*) illustrate the experimental justification for this view:

Compound	$CH_2{:}CHMe$	$CH_2{:}CHEt$	$CH_2{:}CHPr^i$	$CH_2{:}CHBu^t$
ΔH	30·1	30·3	30·3	30·3
Compound	$CH_2{:}CMe_2$	$CH_2{:}CMeEt$	$CH_2{:}CMePr^i$	
ΔH	28·3	28·5	28·0	

In these examples, the mean change in ΔH, on replacement, in the position α- to the ethylenic link, of a C–H bond by a C–C bond, is effectively zero. The groups $-CH_3$, $-CH_2Me$, $-CHMe_2$, and $-CMe_3$ have, therefore, approximately equal effect on the heat of hydrogenation. A conventional interpretation might be that these groups in this system have approximately equal conjugative power.

The existence of hyperconjugation from C–C bonds has been theoretically considered by many workers (cf. Mulliken, Rieke, and Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 41; Hughes, Ingold, Masterman, and McNulty, *J.*, 1940, 899; Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, *J.*, 1948, 2103; Berliner and Berliner, *J. Amer. Chem. Soc.*, 1948, **70**, 854). Its effect on the properties of chemical systems has, however, proved difficult to demonstrate, since it produces electronic movement qualitatively similar to that usually attributed to the inductive effect. Thus, in the bromination of *tert.*-butylbenzene, which is considerably more rapid than that of benzene (de la Mare and Robertson, *J.*, 1943, 279), it is uncertain whether the difference in reactivity is to be ascribed to an inductive effect or to CC-hyperconjugation, the latter view having been favoured by Berliner and Berliner (*loc. cit.*). In a similar way, the large effect of the *tert.*-butyl group, relative to hydrogen, in the comparison below (Hughes, Ingold, and Taher, *J.*, 1940, 949) may result from the inductive effect of the substituent, and the magnitude of any contribution from CC-hyperconjugation cannot at present be determined.

Solvolysis of $R{\cdot}C_6H_4{\cdot}CHPhCl$ in 80% acetone at 0°	R = H	Me	Et	Pr^i	Bu^t
Relative free energy of activation ($RT \log k_R/k_H$, kcal.)	0·0	1·8	1·7	1·5	1·4

No such difficulty arises, however, in attributing the smaller difference between the methyl and *tert.*-butyl compounds to the effect of CH-hyperconjugation. A similar argument applies to consideration of the prototropic systems:

(*a*) $Ph{\cdot}CH_2{\cdot}CH{:}CH_2 \rightleftharpoons Ph{\cdot}CH{:}CH{\cdot}CH_2{\cdot}H$ ..... ΔF * = >4 kcal.
(*b*) $Ph{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CMe_3 \rightleftharpoons Ph{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CMe_3$ ..... ΔF = 2·0 kcal.
(*c*) $Ph{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_3 \rightleftharpoons Ph{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_3$ ..... ΔF = 1·3 kcal.

* The decrease in free energy on transferring 1 g.-mol. from left to right.

The introduction, in (*b*) or (*c*), of either a methyl or a *tert.*-butyl group results in a considerable displacement of the position of equilibrium. As in the similar cases discussed by de la Mare, Hughes, and Ingold (*J.*, 1948, 17), it is clear that CH-hyperconjugation controls the difference between the methyl- and *tert.*-butyl-substituted compounds, in which comparison any contribution from CC-hyperconjugation or from the inductive effect is obscured. The shift in the position of equilibrium on replacing a hydrogen atom

by a *tert.*-butyl group [(*a*) ⟶ (*b*)], however, could be entirely attributable to CC-hyperconjugation, or could be explained by maintaining that the inductive effect of the *tert.*-butyl substituent resists the tendency to allow a proton to attach itself to an adjacent carbon atom. Any combination of these two explanations is allowed, and the use of the "stabilising factor" (*S*) in Treatment 1 does not aid understanding of the results.

The changes in rate coefficients and in equilibrium constants, upon which depend the various demonstrations that CH-hyperconjugation is energetically more important than CC-hyperconjugation (see Crawford, *Quart. Reviews*, 1949, **3**, 226), are usually quite small, the relative rates of the methyl- and *tert.*-butyl-substituted compounds only rarely being equivalent to a difference in free energy of activation of even as much as 0·5 kcal. It is to be expected that inductive and hyperconjugative influences should have different relative importance in different chemical situations: from this arise, for example, the different spheres of influence of the Hofmann and the Saytzeff rule in elimination reactions (Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, *loc. cit.*), and, in the author's opinion, certain of the differences between the effects of substituents on the rates of halogenation and nitration (cf. de la Mare and Robertson, *J.*, 1948, 100). To a first approximation, however, one would expect to find that CH- and CC-hyperconjugations were evoked to the same proportional extent in different situations. It is a real difficulty, then, that, though there is evidence of the preponderating effect of CH-hyperconjugation in, for example, the tautomeric equilibria of the alkylated phenylpropenes, yet no such clear difference is apparent in the studies of the heats of hydrogenation of alkylethylenes.

It seems probable, therefore, that, contrary to conventional interpretations, these heats of hydrogenation are partly subject to inductive influences. For this reason, hypothesis (2*c*) has been expressed in terms of the experimental results, rather than in a derived form depending on a particular theoretical interpretation. At the same time, a further improvement on the earlier treatment is achieved by assuming, in agreement with experiment, that an alkyl group has a smaller effect on the heat of hydrogenation when attached to a phenyl than to a vinyl group. It is assumed also that alkyl groups affect the heat of hydrogenation of systems containing CO_2Et and similar groups by only 1·0 kcal. Kistiakowsky and his co-workers (*locc. cit.*) discussed the following heats of hydrogenation (ΔH, for X = CO_2R):

Compound	Me·CH:CHX	Et·CH:CHX	Me·CH:CH·CH_2X	CH_2:CH·CH_2·CH_2X
ΔH	28·0	27·5	29·6	31·1

They concluded that the extent of conjugation between a double link and a carbethoxy-group is small, but equally methyl-to-vinyl hyperconjugation may have become reduced, when the vinyl group was also conjugated with a carbethoxy-group. That such compounds as CH_3·CH_2·CH:CHX (X = CO_2Me, CO_2^-) are the predominant forms in their equilibria with prototropic isomers CH_3·CH:CH·CH_2X supports the latter view. Bateman and Cunneen's treatment (*loc. cit.*), by stressing the stabilising factor *S*, gives calculated values for the heats of hydrogenation of these compounds which are consistently lower than the experimental values. Better agreement is secured by the present treatment.

A hypothesis such as (2*d*) is necessary because the reduction in the heat of hydrogenation of polymethylethylenes is not proportional to the number of methyl groups introduced. Two methyl groups appear to be about twice as effective as one, but the effect of further methyl groups becomes progressively less. The earlier treatment introduces an analogous, entirely empirical, assumption by using the stabilising factor *S* only twice, whether in 1 : 1-, 1 : 2-, 1 : 1 : 2-, or 1 : 1 : 2 : 2-substituted compounds. In the present treatment, a correction is applied by adding 0·5 kcal. to the calculated heat of hydrogenation (*a*) once for each pair of opposed alkyl groups (*i.e.*, once in 1 : 2-dialkylethylenes, twice in trialkylethylenes, and four times in tetra-alkylethylenes); (*b*) once when the hyperconjugation is crossed with a butadienoid conjugation (*i.e.*, when the alkyl group is placed in the 2- or the 3-position of a conjugated system −C:C·C:C−); (*c*) twice, in systems C:C·CH_2·C:C or C:C·CHR·C:C.

In attempting to assess the success of the two treatments, we consider the experimental results in three sections. First, adequate treatment of the heats of hydrogenation requires

independent knowledge of at least as many experimental values as are assumed in the present treatment. This makes fewer assumptions than the previous analysis, and gives a better fit (as measured by the mean square of the discrepancies between observed and calculated values), both for the compounds considered in the earlier treatment, and for those additional examples quoted in the Appendix.

Appendix

*Observed and Calculated * Energy Differences (kcal.).*

A. *Heats of hydrogenation* (ΔH) *of substituted ethylenes.*

	Found	Calc. (i)	Calc. (ii)
$CH_2{:}CH_2$	32·6	32·6	32·6
$CH_2{:}CHMe$	30·1	30·3	30·2
$CH_2{:}CH{\cdot}CH_2Me$	30·3	30·3	30·5
$CH_2{:}CH{\cdot}CHMe_2$	30·3	30·3	30·8
$CH_2{:}CMe_2$	28·3	28·0	27·8
$CH_2{:}CMe{\cdot}CH_2Me$	28·5	28·0	28·1
$CH_2{:}CMe{\cdot}CHMe_2$	28·0	28·0	28·4
$CH_2Me{\cdot}CH{:}CHMe$	28·0	28·5	28·1
$CMe_2{:}CHMe$	26·9	26·7	26·9
$CMe_2{:}CMe_2$	26·6	25·4	26·0
$CH_2{:}CH{\cdot}CH{:}CH_2$	57·1	57·1	57·1
$CH_2{:}CH{\cdot}CH{:}CHMe$	54·1	54·8	54·7
$CH_2{:}CMe{\cdot}CMe{:}CH_2$	53·9	53·5	52·3
$CH_2{:}CH{\cdot}CH_2{\cdot}CH{:}CH_2$	60·8	61·6	61·0
$CH_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH_2$	60·5	60·6	61·0
$Ph{\cdot}H$	49·8	49·8	49·8
$Ph{\cdot}CH_2Me$	48·9	48·9	49·2
$Ph{\cdot}CH{:}CH_2$	77·5	77·5	77·5
Addenda. Additional compounds relevant to the discussion.			
$CH_2{:}CH{\cdot}CMe_3$	30·3	30·3	(31·1)
$Me{\cdot}CH{:}CH{\cdot}CO_2Et$	28·0	27·8	(26·7)
$Et{\cdot}CH{:}CH{\cdot}CO_2Et$	27·5	27·8	(27·0)
$Me{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2Et$	29·6	29·0	(28·1)
$CH_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$	31·1	30·3	(30·5)
$Me{\cdot}CH{:}CHMe$ (*cis*)	28·5	28·5	(27·8)
$Me{\cdot}CH{:}CHMe$ (*trans*)	27·5	28·5	(27·8)

B. *Free-energy differences* (ΔF) *from the position of equilibrium in the system* $R_1R_2C{:}CR_3{\cdot}CHR_4X \rightleftharpoons R_1R_2CH{\cdot}CR_3{:}CR_4X$.

R_1	R_2	R_3	R_4	X	ΔF (found)	ΔF (i)	ΔF (ii)
H	H	H	H	Ph	>4	4·0	(3·8)
H	CMe_2	H	H	Ph	2·0	2·2	2·0
H	$CHMe_2$	H	H	Ph	1·8	2·2	1·8
H	Me	H	H	Ph	1·3	2·2	1·3
Me	Me	H	H	Ph	0·2	0·4	0·2
H	H	H	H	CO_2^-	2·9	2·5	2·9
H	Me	H	H	CO_2^-	0·6	0·7	0·2
H	Et	H	H	CO_2^-	0·8	0·7	0·5
H	Me	H	Me	CO_2^-	1·1	1·2	1·6
H	Et	H	Me	CO_2^-	1·6	1·2	1·9
H	Me	Me	H	CO_2^-	−0·4	−0·1	0·2
Me	Me	H	H	CO_2^-	−1·0	−1·1	−1·0
H	Me	Et	H	CO_2^-	−1·0	−0·1	0·2
Me	Et	H	H	CO_2^-	−1·0	−1·1	−0·7
H	Me	Me	Me	CO_2^-	0·7	−0·1	1·6
H	Me	Et	Me	CO_2^-	0·0	−0·1	1·6
H	Et	H	H	CO_2Et	1·4	0·7	1·0
H	Et	H	Me	CO_2Et	1·8	1·2	2·4
H	Me	Me	H	CO_2Et	0·7	−0·1	0·7
Me	Me	H	H	CO_2Et	−1·4	−1·1	−0·5
H	Me	Me	Me	CO_2Et	1·6	−0·1	2·1
H	H	H	H	CN	2·3	2·5	3·4
H	Et	H	H	CN	1·1	0·7	1·0
H	Me	Me	H	CN	*2·7*	*−0·1*	*0·7*
Me	Me	H	H	CN	−0·8	−1·1	−0·5

* (i) = This paper; (ii) = Bateman and Cunneen, *J.*, 1951, 2283; values in parentheses have been calculated analogously.

In the second place, the results for the alkyl-phenylpropenes are fitted slightly better by the earlier than by the present treatment in two of the four examples available. This slightly better fit arises partly from the assumption of a different value for the effect of phenyl-to-vinyl conjugation in treating this section of the data, and partly as the result of a subsidiary hypothesis, which assumes a difference between the effectiveness of CC- and CH-hyperconjugation. Since this difference does not appear in the heats of hydrogenation, it must be impossible to interpret in a consistent manner the two sets of data without introducing some further subsidiary hypothesis. To take account of the difference between the observed effects of alkyl substituents in the two systems, therefore, a further degree of approximation than that of the treatment now preferred would be required.†

In the third place, the present treatment fits the data for acids, esters, and nitriles slightly better, if the italicised value for $CH_2Me{\cdot}CMe{:}CH{\cdot}CN$ is neglected, but slightly worse if this value is included. The error of estimate in each treatment is larger for this than for any other compound, and Bateman and Cunneen (*loc. cit.*) give a special explanation in terms of the mutual inductive influences of the methyl and cyano-substituents. In the author's view, a similar discrepancy would then have been expected in the analogous compound containing, in place of CN, the CO_2Et group which must also exert a very

† For a similar reason, we have neglected, among other factors which may sometimes be important: (i) steric requirements of hyperconjugation (cf. Baddeley, Chadwick, and Rawlinson, *Nature*, 1949, **164**, 833); (ii) the effect of polar groupings in changing the hyperconjugative power of the C–H bonds in CH_2X (cf. Robertson, Heyes, and Swedlund, *J.*, 1952, in the press); (iii) hyperconjugation of the type $CH_2{=}CH{-}CH_2{-}X$ (cf. de la Mare, Hughes, and Ingold, *loc. cit.*).

strong inductive effect. Such a discrepancy is not observed, however, and therefore there seems to be no satisfactory explanation of the anomaly in terms of either treatment. Extension of the data relating to esters and cyanides to include further examples would seem to be required to solve this difficulty.

The position of equilibrium in the system $CH_3{\cdot}CHBr{\cdot}CH{:}CH_2 \rightleftharpoons CH_3{\cdot}CH{:}CH{\cdot}CH_2Br$ (ΔF: Found, 1·3. Calc., 1·8) is reasonably well explained on the scheme now preferred; there is no evidence to allow assessment of the effect which Bateman and Cunneen (*loc. cit.*) propose in this case. The bond energies of propane and propylene, compared with those of ethane and ethylene, are also understandable; in dissociating the C–Me bond in propylene, the energy of methyl-to-vinyl hyperconjugation (about 2·3 kcal., in the present estimate) is lost, whereas hyperconjugation of this type is not found in the other compounds.

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William Ramsay and Ralph Forster Laboratories, University College, Gower Street, London, W.C.1. [*Received, December 11th*, 1951.]

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295. *Ion-exchange Resins as Catalysts in the Hydrolysis of Esters.*

By C. W. Davies and G. Garrod Thomas.

Rate constants and apparent activation energies are reported for the hydrolysis of a number of esters, catalysed in aqueous solution by ion-exchange resins in the hydrogen form. For equivalent amounts, the resins are more effective catalysts than hydrochloric acid, and increasingly so as the molecular weight of the ester increases. An explanation is offered for the apparent conflict between these results and those of Haskell and Hammett.

The catalysts of ester hydrolysis by exchange resins was the subject of a note by us some years ago (*Nature*, 1947, **159**, 732). Since then Haskell and Hammett (*J. Amer. Chem. Soc.*, 1949, **71**, 1284) have published the results of some studies in the same field which, at first sight, seem to lead to conclusions almost diametrically opposed to ours. The object of the present paper is to place our data on record, and to put forward an explanation of the apparent discrepancy.

Experimental

Materials.—Two resins were used, Amberlite IR-100 (20—60 mesh) and Wofatit C. Two particle sizes were employed with the latter, 20—40 mesh and 40—60 mesh. The resins were regenerated with 2N-hydrochloric acid, thoroughly washed, and air-dried. Their moisture contents were determined by heating samples for two days at 130°. The esters were purified by storage over sodium carbonate and then over anhydrous calcium chloride, followed by distillation.

Method.—In a few experiments the proportions of resin, ester, and water were varied. Usually, however, 50 ml. of water and 2 ml. of ester were employed, with 1 g. of Amberlite IR-100 or 2 g. of the weakly acid Wofatit. The reaction mixtures were contained in 100-ml. glass-stoppered bottles which were suspended in a thermostat controlled to within 0·05° (0·10° at 55°), and agitated by a device similar to that described by Willcocks (*J. Soc. Chem. Ind.*, 1938, **57**, 249). The resin–water mixture was allowed to come to temperature equilibrium, and the ester (at the same temperature) was added. After measured times, bottles were opened, 25 ml. (usually) of the aqueous phase were withdrawn, and the liberated acetic acid was titrated against standard barium hydroxide (phenolphthalein). The titre corresponding to complete hydrolysis was checked by control experiments, and preliminary experiments showed that the adsorption of acetic acid by the resin was negligible.

Where the ester was completely soluble at the concentrations used, the volume of solution

was taken to be the sum of the volumes of the added water and ester plus the water originally present in the resin. First-order constants were calculated from the expression

$$k_1 = (2{\cdot}303/wt) \log T_\infty/(T_\infty - T_t)$$

where w is the weight (in g.) of dry resin, t the time (in seconds), T_t the titre at time t, and T_∞ that corresponding to total hydrolysis of the sample withdrawn (assuming uniform distribution, *i.e.*, negligible adsorption by the resin of the ester). Table 1 shows the course of a typical series of experiments.

TABLE 1. *Hydrolysis of ethyl acetate with Amberlite* IR-100 *at* 25°.

Wt. of dry resin, 0·6635 g. Initial ester concn., 0·3925M. 10-Ml. samples titrated. T_∞ = 66·24 ml.

t, hours	10·52	18·93	42·53	47·45	53·73	64·48	71·38	74·53	94·60	116·0	360
T_t	13·41	22·80	40·75	43·42	46·41	50·79	52·84	53·70	57·90	60·20	63·13
$k_1 \times 10^6$	9·02	9·33	9·40	9·40	9·40	9·45	9·38	9·35	9·18	8·65	—

With the less soluble esters a separate ester phase was visible during the greater part of the reaction, and in these cases zero-order constants were calculated: k_0 = moles hydrolysed per g. of dry resin per second. Blank experiments in which aqueous acetic acid solutions were shaken with the appropriate ester provided small corrections for the volume change resulting from ester passing into the aqueous phase, and from acetic acid being retained in the ester phase. Table 2 gives details of a typical experiment.

TABLE 2. *Hydrolysis of* n-*amyl acetate with Amberlite* IR-100 *at* 25°.

Wt. of dry resin, 0·6640 g. 25-Ml. samples titrated with 0·1192N-barium hydroxide.

t, hours	8·80	13·93	24·58	36·87	46·18	69·05	86·65	109·23
T_t	3·91	6·54	11·50	16·78	21·17	30·00	35·93	42·10
$k_0 \times 10^8$	4·52	4·77	4·75	4·63	4·66	4·41	3·20	3·01

RESULTS AND DISCUSSION

In earlier work (Davies and Thomas, *J.*, 1951, 2624) we had found that organic acids are positively adsorbed on the resins used here. With acids of low molecular weight, however, the extent of adsorption was relatively slight, and at moderate concentrations the amount of acid at the resin surface was almost proportional to its concentration in the outer solution. We expected that simple ester molecules would show similar behaviour, so that the amount undergoing hydrolysis at the resin surface would show an approximately linear dependence on the concentration of ester in solution. That this is so is shown by the satisfactory first-order constant in the typical series recorded in Table 1. Where the added ester was not wholly soluble in the aqueous phase, a zero-order constant such as that shown in Table 2 was obtained, expressing the rate of hydrolysis in a surface layer which was in equilibrium with a saturated aqueous solution of the ester; the resin was without influence on the excess of undissolved ester.

In some experiments the amount of resin was varied. 2 Ml. of methyl acetate and 50 ml. of water being used with Amberlite IR-100 at 25°, the first-order constants (per g. of resin) obtained with 0·5, 1·0, and 2·0 g. of air-dried resin were, respectively, $7{\cdot}56$, $7{\cdot}38$, and $6{\cdot}90 \times 10^{-6}$. This decrease in reaction rate would be consistent with an adsorption of approximately 1 milli-equiv. of ester per g. of resin. With *n*-butyl acetate, when a separate ester phase was present, the rate constant was unaffected by change in the amount of resin.

When the amount of ester was varied, the rate constant was again affected. For example, on doubling of the concentration of methyl acetate the value $7{\cdot}38 \times 10^{-6}$, just quoted, fell to $6{\cdot}33 \times 10^{-6}$. This decrease would be expected on the basis of an adsorption isotherm of the type found for organic acids (Davies and Thomas, *loc. cit.*), the concentration in the adsorbed layer being less than doubled. In accordance with expectation, the zero-order constants for *n*-butyl and *n*-amyl acetates were unaffected by varying the amount of ester.

The effect of particle size was studied in the hydrolysis of *n*-butyl acetate by Wofatit C. The zero-order constant was 6% higher for 40—60 mesh resin than for the 20—40 mesh size. Similar data have been reported by Haskell and Hammett (*loc. cit.*). The results

suggest that the outer layers of the resin granules are responsible for much of the catalytic effect, the diffusion of non-electrolytes towards or away from the centre of the particles being a slow process. The same conclusion was reached in our earlier paper on adsorption and desorption rates. It will be noticed in Table 1 that the rate constant falls off towards the end of the reaction. This was a general phenomenon, and suggests that the reaction is somewhat retarded, as might be expected, by its products. This probably applies particularly to the interior of the granules as acid and alcohol molecules accumulate.

Our results are collected in Tables 3 and 4. The constants given here are comparable, in so far as uniform amounts of ester, water, and resin were used and the resin samples were taken from a common stock.

The values of r in Table 4 give the ratio of the constant found for Amberlite IR-100 (20—60 mesh) to that for Wofatit C (20—40 mesh). The figures are reasonably constant, and show that Amberlite IR-100, containing 2 milli-equivs. of sulphonic groups per g., is about 11 times more efficient as a catalyst than the Wofatit C, which contained approximately 4 milli-equivs. of carboxyl groups per g. Strong acid Amberlites possessing both higher capacity and greater stability than the IR-100 resin are now, of course, available.

The rate constants of Table 3 may be compared with the constants previously obtained for homogeneous catalysis by hydrochloric acid at similar ester concentrations. For methyl acetate at 25° we used the data of Griffiths and Lewis (*J.*, 1916, **109**, 67) and for

TABLE 3. *Amberlite* IR-100 *as catalyst.*

	$k_1 \times 10^6$		$k_0 \times 10^6$		
Temp.	MeOAc	EtOAc	BuOAc	AmOAc	CH_2Ph·OAc
15°	2·87	3·50	4·11	2·15	—
25	7·38	9·40	9·47	4·72	5·28
35	18·3	22·7	19·6	9·20	—
45	—	49·2	38·6	—	—
55	—	97·8	—	—	—

TABLE 4. *Wofatit C as catalyst.*

	$k_1 \times 10^6$		$k_0 \times 10^6$			$k_1 \times 10^6$		$k_0 \times 10^6$	
Temp.	EtOAc	r	BuOAc	r	Temp.	EtOAc	r	BuOAc	r
15°	—	—	0·356	11·6	35°	2·05	11·1	1·85	10·6
25	0·860	10·9	0·861	11·0					

ethyl acetate those of Harned and Pfanstiel (*J. Amer. Chem. Soc.*, 1922, **44**, 2193). For the sparingly soluble esters our results were compared with calculated rates for the homogeneous catalysis of saturated aqueous solutions, the velocity data of Palomaa (*Chem. Z.*, 1913, **84**, 1956) being used for butyl acetate and those of Smith and Paterson (*J.*, 1926, 940) for benzoyl acetate. The solubility of butyl acetate was taken from Hodgman ("Handbook of Chemistry and Physics," 32nd edn., p. 666). The comparison shows that the resin is more effective than hydrochloric acid by factors of 1·8 for methyl acetate, 2·3 for ethyl acetate, 10 for *n*-butyl acetate, and 20 for benzyl acetate. These results are reasonable in view of the other evidence that the esters are positively adsorbed at the active surface, and the probability that the amount adsorbed, for the esters as for the organic acids, increases rapidly with increasing molecular weight.

The results of Haskell and Hammett (*loc. cit.*) appear, at first sight, to be almost exactly the reverse of ours. These authors studied the hydrolysis of methyl and ethyl acetates, ethyl *n*-butyrate, and ethyl *n*-hexanoate dissolved in 70% acetone (*a*) in the presence of Amberlite IR-120, and (*b*) with an equivalent amount of hydrochloric acid. They found that hydrochloric acid was catalytically more efficient than the resin by factors of approximately 2 for methyl acetate, 3 for ethyl acetate, 7·5 for ethyl butyrate, and 20 for ethyl hexanoate. The two sets of results, though apparently so divergent, can both find a simple common explanation, along the lines we have used in discussing our own, if it is supposed that in 70% acetone the esters are negatively adsorbed by the resin: that is, the ester concentration is *less* in the resin than in the body of the solution, and increasingly so with increasing molecular weight. Evidence for this supposition is supplied by Haskell

and Hammett's Table 6, in which they show that solvent is adsorbed by the resin in preference to hexanoic or acetic acid, and that the effect is greater for the former.

The opposite effects, both in catalytic efficiency and in adsorbability, revealed by the two sets of results are clearly due to the change of solvent from water to 70% acetone, and an insight into the striking effect of this change is provided by some results recently obtained in these laboratories. B. D. R. Owen (unpublished) has found that when 10% divinylbenzene cross-linked polystyrene resin in the hydrogen form is equilibrated with a 70% acetone in water mixture, in the proportions used by Haskell and Hammett, the liquid absorbed by the resin has the composition 72% water, 28% acetone, the composition of the outer solution now being 75% acetone, 25% water. The distribution of the organic substrate between these two phases will be greatly in favour of the outer solution—especially for long-chain esters which are sparingly soluble in water—and thus provides an explanation both for the negative adsorptions and for the low catalytic activities found by Haskell and Hammett.

When the rate constants of Tables 3 and 4 are plotted against the reciprocal of the absolute temperature straight lines are obtained, and the slopes of these give the values of apparent activation energies (in cal.) recorded below. There is a marked drop in the apparent activation energy as the chain length increases. The temperature influence is

Ester	Amberlite IR-100	Wofatit C	HCl	Ester	Amberlite IR-100	Wofatit C	HCl
Methyl acetate	16,600	—	16,920	*n*-Butyl acetate	13,180	13,960	—
Ethyl acetate	15,540	15,810	16,830	*n*-Amyl acetate	12,280	—	—

not easy to interpret quantitatively, however, as not only the reaction mechanism itself but also the adsorption energy and, to a lesser degree, swelling and diffusion effects are involved.

We thank the Department of Scientific and Industrial Research for the award of a maintenance allowance, and the Chemical Research Laboratory and Messrs. Charles Lennig & Co., Ltd., 18—20, York Buildings, London, W.C.2, for gifts of resins.

EDWARD DAVIES CHEMICAL LABORATORIES,
ABERYSTWYTH, WALES. [*Received, December 10th*, 1951.]

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296. *Studies on the Diels–Alder Reaction. Part II.* The Reaction between Methylvinylcyclohexene and Benzoquinone.*

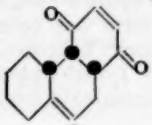
By P. A. ROBINS and JAMES WALKER.

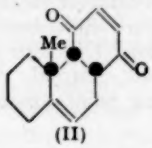
Specimens of methylvinyl*cyclo*hexene, derived from the solid and liquid geometrically stereoisomeric forms of 1-ethynyl-2-methyl*cyclo*hexanol, appear to consist of mixtures of isomeric dienes, 1-methyl-2-vinyl- (III) and 3-methyl-2-vinyl-*cyclo*hexene (IV), of which only the latter participates with benzoquinone in the Diels–Alder reaction, giving $\Delta^{2:9(14)}$-decahydro-1 : 4-diketo-8-methylphenanthrene (VII). The structure of (VII) was proved by conversion into 1-methyl- and 1 : 8-dimethyl-phenanthrene, and a number of reduction products are described.

IN a previous paper * we have described the Diels–Alder reaction between 1-vinyl*cyclo*hexene and benzoquinone, together with a study of the reduction, under a variety of conditions, of the resulting $\Delta^{2:9(14)}$-decahydro-1 : 4-diketophenanthrene (I). This work has now been extended with the intention of studying the 13-methyl homologue (II), which, however, we have not yet succeeded in obtaining. For the synthesis of (II), authentic 1-methyl-2-vinyl*cyclo*hexene (III) was required, and, notwithstanding the paucity of examples in the literature of the successful use of 1 : 1-disubstituted butadienes in the Diels–Alder reaction (cf. Kloetzel, *Org. Reactions*, **4**, 1; Holmes, *ibid.*, p. 60; Butz, *ibid.*, **5**, 136), there seemed good reason, in view of the seemingly convincing work of Wang

* Part I, *J.*, 1952, 642.

and Hu (*J. Chinese Chem. Soc.*, 1943, **10**, 1) discussed below, to believe that (II) would result from the Diels–Alder reaction between (III) and benzoquinone.


(I)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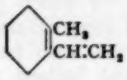
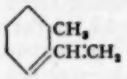

(III)

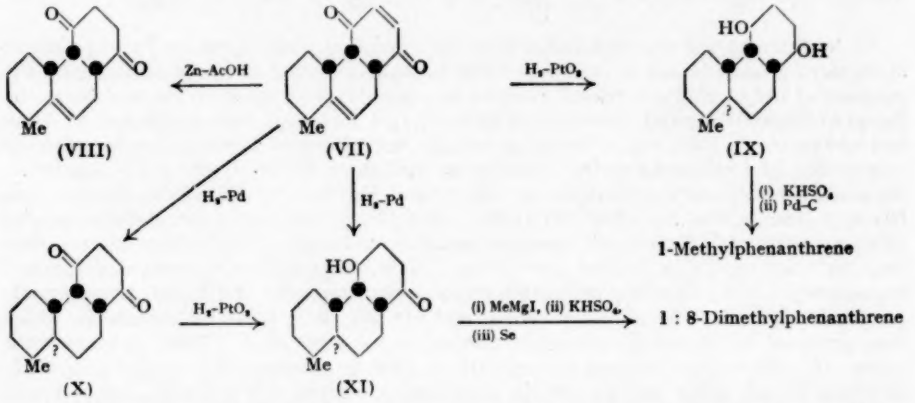

(IV)

In addition to the experimental difficulties associated with obtaining pure specimens of vinyl*cyclo*hexene for use in the Diels–Alder reaction, discussed in our previous paper, the presence of the methyl substituent introduces a possibility of structural isomerism in the diene, which, as Wang and Hu indicated (*loc. cit.*), had previously been overlooked (cf. Cook and Lawrence, *J.*, 1938, 58). Two geometrically stereoisomeric forms are produced in the preparation of 1-ethynyl-2-methyl*cyclo*hexanol and these are relatively easily separated, since one is a solid and crystallises out (Wang and Hu, *loc. cit.*; Milas, MacDonald, and Black, *J. Amer. Chem. Soc.*, 1948, **70**, 1829). On hydrogenation these two stereoisomerides afford stereoisomeric 2-methyl-1-vinyl*cyclo*hexanols, and these, on dehydration, give what may for convenience be termed methylvinyl*cyclo*hexene-*s* and methylvinyl*cyclo*hexene-*l* respectively, *s* and *l* denoting derivation respectively from *s*olid and *l*iquid stereoisomeric acetylenic alcohols. According to Wang and Hu (*loc. cit.*), these hydrocarbons, which they prepared by essentially the same method as we have used, yielded products with maleic anhydride which passed respectively on dehydrogenation into naphthalene-1 : 2-dicarboxylic anhydride and its 5-methyl derivative. From this evidence, methylvinyl-*cyclo*hexene-*s* would appear to be 2-methyl-1-vinyl*cyclo*hexene (III) and methylvinyl-*cyclo*hexene-*l* to be 3-methyl-2-vinyl*cyclo*hexene (IV), and, on the basis of *trans*-elimination of water, the solid acetylenic alcohol would thus appear to have the *trans*- and the liquid form the *cis*-structure. These configurations for the acetylenic alcohols are, however, contrary to those assigned by Milas *et al.* (*loc. cit.*) on the basis of the relative yields of the ethynyl*cyclo*hexenes obtained on dehydration over aluminium phosphate at 290—295°. Moreover, it may be noted that essentially the same ethynylmethyl*cyclo*hexene (V) was obtained by Milas and his collaborators from both alcohols since ozonolysis of enyne-*s* and of enyne-*l* gave in each case 6-ketoheptanoic acid (VI).

(V) $\longrightarrow$ $CH_3 \cdot CO \cdot [CH_2]_4 \cdot CO_2H$ (VI)

On allowing our methylvinyl*cyclo*hexene-*s* and -*l* to react with benzoquinone, we obtained comparable yields in the two cases of the same $\Delta^{2:9(14)}$-decahydro-1 : 4-diketomethylphenanthrene, which further study has conclusively shown to be the 8-methyl derivative (VII), and not (II), since it could be converted, as described below, into 1-methyl- and 1 : 8-dimethyl-phenanthrene. Furthermore, as only (VII) was obtained and no other decahydrodiketomethylphenanthrene could be isolated, it is obvious that, under the relatively standard conditions used, the specimens of methylvinyl*cyclo*hexene-*s* and -*l*, which we had obtained, were probably similar mixtures of (III) and (IV), of which only the latter participated readily in the Diels–Alder reaction with benzoquinone, giving (VII). In order to ascertain whether the 2-methyl-1-vinyl*cyclo*hexene (III) would react under more vigorous conditions, addition of benzoquinone to diene-*s* was carried out in boiling benzene : the sole product was (VII). Attempts to increase the vigour of the conditions, *e.g.*, by use of a benzene solution at 100° in a sealed vessel, gave only dark brown tarry products from which no recognisable material could be isolated. One may conclude therefore that, if benzoquinone is to be used to furnish ring C in a steroid synthesis, it will be essential to avoid the use of a 1 : 1-disubstituted diene in any Diels–Alder reaction intended for this purpose and to attach rings B and A, as well as, of course, ring D, in separate stages.

By the techniques described in our previous paper, reduction of (VII) with zinc and acetic acid gave $\Delta^{9(14)}$-dodecahydro-1 : 4-diketo-8-methylphenanthrene (VIII), and perhydrogenation in the presence of Adams's catalyst yielded perhydro-1 : 4-dihydroxy-8-methylphenanthrene (IX), of which one pure stereoisomeric form has been isolated. Dehydration of the mixed stereoisomeric diols (IX) with potassium hydrogen sulphate, followed by dehydrogenation with palladised charcoal, yielded 1-methylphenanthrene, having characteristically the highest melting point among monomethylphenanthrenes.



Hydrogenation of (VII) in the presence of palladised strontium carbonate gave perhydro-1 : 4-diketo-8-methylphenanthrene (X), when stopped at the appropriate stage, or perhydro-4-hydroxy-1-keto-8-methylphenanthrene (XI), when prolonged until the appropriate volume of hydrogen had been absorbed. The hydroxy-ketone (XI) was, however, more conveniently prepared by hydrogenation of the diketone (X) in the presence of Adams's catalyst. The structure of (XI) was demonstrated by marking the position of the carbonyl group by the Grignard reagent, whereafter dehydration and dehydrogenation of the resulting perhydro-1 : 4-dihydroxy-1 : 8-dimethylphenanthrene afforded 1 : 8-dimethylphenanthrene, which, incidentally, has the highest melting point among the 17 dimethylphenanthrenes hitherto described.

Experimental

2-*Methyl*cyclo*hexanol*.—*o*-Cresol (500 g.), containing metallic sodium (0·3 g.), was hydrogenated at 80°/110 atm. (initial) in the presence of Raney nickel (*ca.* 20 g.) (cf. Ungnade and Nightingale, *J. Amer. Chem. Soc.*, 1944, **66**, 1218). Absorption of hydrogen was rapid and exothermic, the temperature rising to ~200°. The hydrogenated product, after dilution with benzene (500 c.c.), was filtered from the catalyst, washed once with 2N-sodium hydroxide, and fractionated, giving 2-methyl*cyclo*hexanol (485 g., 95%), b. p. 74—76°/20 mm.

2-*Methyl*cyclo*hexanone*.—2-Methyl*cyclo*hexanol (260 g.) was added slowly to a vigorously stirred solution of sodium dichromate (120 g.) and concentrated sulphuric acid (100 g.) in water (600 c.c.). A cooling-bath was used intermittently to keep the temperature of the reaction mixture below 50°. At the end of the reaction the mixture was stirred until cool and then extracted with ether. The ethereal solution was washed with 5% aqueous sodium hydroxide (3 × 200 c.c.), dried, and fractionated, giving 2-methyl*cyclo*hexanone (178 g., 70%), b. p. 62°/21 mm., n_D^{20} 1·4522 (lit., b. p. 59—60°/20 mm., n_D^{15} 1·450).

1-*Ethynyl*-2-*methyl*cyclo*hexanol*.—Condensation of 2-methyl*cyclo*hexanone and sodium acetylide in liquid ammonia as for 1-ethynyl*cyclo*hexanol (*J.*, 1952, 646) gave the alcohol (75—87%), b. p. 77°/13 mm. When kept at 0°, the distilled liquid partly solidified and filtration gave the solid isomer, which, after crystallisation from a small volume of light petroleum, had m. p. 56—58°; about 30% of the distilled material could be obtained as a solid. Milas *et al.* (*J. Amer. Chem. Soc.*, 1948, **70**, 1829) record m. p. 61—61·5° for the solid stereoisomer obtained in 50% yield.

Partial Hydrogenation of the Stereoisomeric 1-*Ethynyl*-2-*methyl*cyclo*hexanols*.—1-Ethynyl-2-methyl*cyclo*hexanol (85 g.; m. p. 55°) was hydrogenated at room temperature and atmospheric pressure in methanol (1 l.) in the presence of 2% palladised strontium carbonate (5 g.), until the solution just failed to give a precipitate with alcoholic silver nitrate solution. After removal of the catalyst, fractionation afforded 2-methyl-1-vinyl*cyclo*hexanol-*s* (79 g.), b. p. 79—80°/15 mm., n_D^{19} 1·4830 (Found: C, 77·0; H, 11·4. Calc. for $C_9H_{16}O$: C, 77·2; H, 11·4%). Wang and Hu (*loc. cit.*) record b. p. 66—67°/10 mm.

Similar treatment of the stereoisomeric liquid 1-ethynyl-2-methyl*cyclo*hexanol (170 g.) afforded the stereoisomeric 2-methyl-1-vinyl*cyclo*hexanol-*l* (159 g.), b. p. 74—75°/11 mm., n_D^{23} 1·4760 (Found: C, 77·2; H, 11·6%). Wang and Hu (*loc. cit.*) record b. p. 75—76°/16 mm.

Dehydration of the Stereoisomeric 2-*Methyl*-1-*vinyl*cyclo*hexanols*.—2-Methyl-1-vinyl*cyclo*hexanol-*s* (30 g.) was slowly distilled in a stream of nitrogen from powdered anhydrous potassium hydrogen sulphate (5 g.), heated to 180° in an oil-bath. The distillate, separated from the aqueous layer and dried (K_2CO_3), was redistilled from a little anhydrous potassium hydrogen sulphate, giving crude methylvinyl*cyclo*hexene-*s* (21 g., 80%), b. p. 156—157°, n_D^{19} 1·4978. Careful fractionation of the crude diene showed that, although it distilled almost entirely over a very narrow temperature range, the refractive indices of the fractions varied considerably. The crude diene was therefore used without further investigation in the subsequent reaction with benzoquinone.

In a like manner, the stereoisomeric 2-methyl-1-vinyl*cyclo*hexanol-*l* (15 g.) was dehydrated, to give an inhomogeneous sample of methylvinyl*cyclo*hexene-*l* (11·7 g.), b. p. 155—157°, n_D^{19} 1·4895.

$\Delta^{2:9(14)}$-*Decahydro*-1 : 4-*diketo*-8-*methylphenanthrene* (VII).—Crude methylvinyl*cyclo*hexene-*s* (8·3 g.) in methanol (30 c.c.) was treated with benzoquinone (3 g., 0·38 mol.; the use of a molecular proportion of benzoquinone interfered with the subsequent isolation of the product). After swirling to effect dissolution of the benzoquinone, the reaction mixture became warm and a pale yellow crystalline solid separated. After 18 hours at room temperature, the reaction mixture was cooled to −5° and filtered, yielding $\Delta^{2:9(14)}$-*decahydro*-1 : 4-*diketo*-8-*methylphenanthrene* (VII) (3·9 g.), m. p. 125—126°, in the form of pale yellow leaflets; light absorption in ethanol, $\lambda_{max.}$ 225, 290, 340 mμ (log ε = 4·08, 2·20, 1·90) (Found: C, 78·3; H, 7·9. $C_{15}H_{16}O_2$ requires C, 78·2; H, 7·9%). The observed light-absorption characteristics were practically identical with those recorded previously for the lower homologue (*J.*, 1952, 646).

Similar reaction of crude methylvinyl*cyclo*hexene-*l* (8·3 g.) in methanol (30 c.c.) with benzoquinone (3 g.) gave $\Delta^{2:9(14)}$-decahydro-1 : 4-diketo-8-methylphenanthrene (3·12 g.), identical with that described above.

Reaction of methylvinyl*cyclo*hexene-*s* (4·0 g.) with benzoquinone (3·0 g.) in boiling benzene (25 c.c.) for 2·5 hours gave, after evaporation of the solvent and removal of unchanged benzoquinone and diene at 100° *in vacuo*, almost pure $\Delta^{2:9(14)}$-decahydro-1 : 4-diketo-8-methylphenanthrene (1·70 g., 22·5% calc. on the diene). No other non-volatile product could be detected.

$\Delta^{9(14)}$-*Dodecahydro*-1 : 4-*diketo*-8-*methylphenanthrene* (VIII).—$\Delta^{2:9(14)}$-Decahydro-1 : 4-diketo-8-methylphenanthrene (1·0 g.) in glacial acetic acid (50 c.c.) was treated with zinc powder (1·0 g.), and the reaction mixture was stirred for 10 minutes at room temperature. Ether (50 c.c.) was added and the zinc acetate together with unused zinc removed by filtration. Evaporation of the filtrate under reduced pressure at below 50° gave a solid residue, which, on extraction with boiling light petroleum, afforded colourless prisms of $\Delta^{9(14)}$-*dodecahydro*-1 : 4-*diketo*-8-*methylphenanthrene* (VIII), m. p. 122—123° (Found: C, 77·9; H, 9·1. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·7%).

Perhydrogenation of $\Delta^{2:9(14)}$-*Decahydro*-1 : 4-*diketo*-8-*methylphenanthrene* (VII) *in Ethyl Acetate Solution. Perhydro*-1 : 4-*dihydroxy*-8-*methylphenanthrene* (IX).—A solution of the decahydrodiketomethylphenanthrene (VII) (1·0 g.) in ethyl acetate (80 c.c.) containing perchloric acid (2 drops of 70%) was shaken with Adams's platinum oxide catalyst (50 mg.) in hydrogen at atmospheric pressure and room temperature until absorption of hydrogen ceased (8 hours for 4·5 mols.). After removal of the catalyst the solution was concentrated to small bulk and addition of much light petroleum then gave a white crystalline solid. Recrystallisation from benzene–ethanol afforded fine colourless needles (0·12 g.) of *perhydro*-1 : 4-*dihydroxy*-8-*methylphenanthrene* (IX), m. p. 195° (Found: C, 75·9; H, 10·6. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%). No further solid product could be isolated.

Degradation of (VII) *to* 1-*Methylphenanthrene*.—$\Delta^{2:9(14)}$-Decahydro-1 : 4-diketo-8-methylphenanthrene (VII) (2 g.) was hydrogenated at atmospheric pressure and room temperature in glacial acetic acid in the presence of Adams's platinum oxide catalyst (0·2 g.). After 5½ hours

absorption of hydrogen had ceased, approximately 3·6 mols. having been absorbed. Removal of the catalyst and evaporation gave a clear gum consisting essentially of a mixture of stereoisomeric perhydro-1 : 4-dihydroxy-8-methylphenanthrenes. The gum was mixed with powdered anhydrous potassium hydrogen sulphate (8 g.) and the mixture was heated in an atmosphere of nitrogen to 180—200° for 45 minutes. After cooling, the reaction mixture was distributed between water and low-boiling light petroleum, and the organic layer was dried (Na_2SO_4) and allowed to percolate down a short column of activated alumina (Peter Spence and Sons, type H). The effluent, together with low-boiling light petroleum washings, was evaporated to dryness, to give a pale yellow mobile oil (1·3 g.) which gave a strong brown colour with tetranitromethane.

The oil (0·7 g.) was heated with 5% palladised charcoal (1 g.) in boiling diphenylamine (5 g.) until no further evolution of gas took place, about 5 hours being required. After cooling, the reaction mixture was taken up in ether and filtered to remove the catalyst. The filtrate was saturated with dry hydrogen chloride, and the precipitated diphenylamine hydrochloride was collected and washed with ether. On evaporation of the filtrate and washings to dryness, the residue, which solidified readily but still contained traces of diphenylamine, was taken up in low-boiling light petroleum and allowed to percolate through a short column of activated alumina. The effluent and washings, on evaporation, gave a solid residue, which, after one recrystallisation from methanol, afforded shining colourless plates of 1-methylphenanthrene (0·36 g.), m. p. 118—119° (styphnate, m. p. 149—150°). Haworth (*J.*, 1932, 1125) records 1-methylphenanthrene, m. p. 118°, and its styphnate, m. p. 149—150°.

Perhydro-1 : 4-*diketo*-8-*methylphenanthrene* (X).—A solution of $\Delta^{2:9(14)}$-decahydro-1 : 4-diketo-8-methylphenanthrene (VII) (500 mg.) in methanol (100 c.c.) was shaken with 2% palladised strontium carbonate (0·5 g.) in hydrogen at atmospheric temperature and pressure until two molecular proportions of hydrogen had been absorbed, 70 minutes being required. After filtration and removal of the solvent, the residue, crystallised from aqueous methanol, gave colourless needles (280 mg.) of *perhydro*-1 : 4-*diketo*-8-*methylphenanthrene* (X), m. p. 140—141° (Found : C, 76·9; H, 9·2. $C_{15}H_{22}O_2$ requires C, 77·1; H, 9·5%).

Perhydro-4-*hydroxy*-1-*keto*-8-*methylphenanthrene* (XI).—Perhydro-1 : 4-diketo-8-methylphenanthrene (X) (1·95 g.) in methanol (100 c.c.) was shaken in hydrogen at atmospheric pressure and room temperature with Adams's platinum oxide catalyst (100 mg.) for 42 hours, one mol. of hydrogen being absorbed. After removal of the catalyst and evaporation of the solvent, recrystallisation of the residue from light petroleum–ethyl acetate gave fine colourless needles of *perhydro*-4-*hydroxy*-1-*keto*-8-*methylphenanthrene* (XI) (1·50 g.), m. p. 125—126° (Found : C, 76·5; H, 10·2. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%).

The 2 : 4-*dinitrophenylhydrazone* separated from toluene in orange needles, m. p. 190—193° (Found : C, 60·8; H, 6·8; N, 13·2. $C_{21}H_{28}O_5N_4$ requires C, 60·5; H, 6·8; N, 13·5%).

The hydroxy-ketone (XI) could also be obtained in 56% yield by hydrogenation of (VII) in methanol in the presence of palladised strontium carbonate but the uptake of hydrogen became extremely slow at the last stage.

Perhydro-1 : 4-*dihydroxy*-1 : 8-*dimethylphenanthrene*.—The above hydroxy-ketone (XI) (1·0 g.) was added in dry benzene (40 c.c.) to a boiling stirred solution of methylmagnesium iodide (from 2·0 g. of magnesium and 11·5 g. of methyl iodide) in benzene (100 c.c.). After being stirred under reflux for 5 hours, the reaction mixture was cooled in ice and decomposed with 2N-sulphuric acid (80 c.c.). The organic layer was separated and the aqueous phase was extracted once with ether. The combined organic layers were washed with water, dried (Na_2SO_4), and evaporated. The residue, which solidified spontaneously, was recrystallised from ethyl acetate–light petroleum, affording colourless prisms (0·55 g.) of *perhydro*-1 : 4-*dihydroxy*-1 : 8-*dimethylphenanthrene*, m. p. 155—156° (Found, on a sample dried at 140°/20 mm. : C, 76·2; H, 11·2. $C_{16}H_{28}O_2$ requires C, 76·1; H, 11·2%).

1 : 8-*Dimethylphenanthrene*.—The above perhydro-1 : 4-dihydroxy-1 : 8-dimethylphenanthrene (0·52 g.), mixed with powdered anhydrous potassium hydrogen sulphate (5 g.), was heated at *ca.* 180° under nitrogen for 45 minutes. After cooling and addition of water, the organic material was extracted with low-boiling light petroleum. The petroleum solution was dried (Na_2SO_4) and allowed to percolate down a short column of activated alumina, and effluent and washings on evaporation yielded a colourless oil (0·4 g.), giving a strong brown colour with tetranitromethane.

The oil was heated in a sealed tube with selenium (1·2 g.) at 345° for 42 hours. After cooling, the tube was cautiously opened in view of the internal pressure and the contents were washed out with much ether. Evaporation of the filtered ethereal solution afforded a solid residue, m. p. 140—160°, which was sublimed at 180—200°/20 mm. Five crystallisations from glacial

acetic acid afforded glittering plates of 1 : 8-dimethylphenanthrene (100 mg.), m. p. 187—190°, not depressed on admixture with an authentic specimen, m. p. 190—191°, kindly provided by Professor R. D. Haworth, F.R.S. (cf. Haworth, Mavin, and Sheldrick, *J.*, 1934, 454) (Found: C, 93·4; H, 6·8. Calc. for $C_{16}H_{14}$: C, 93·2; H, 6·8%).

The authors are again indebted to Mr. W. A. L. Marshment for technical assistance.

NATIONAL INSTITUTE FOR MEDICAL RESEARCH,
THE RIDGEWAY, MILL HILL, LONDON, N.W.7. [*Received, December 28th*, 1951.]

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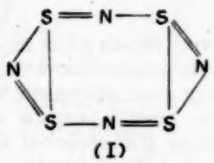
297. *The Structure of Sulphur Nitride.*

By D. CLARK.

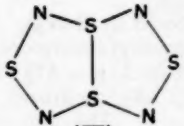
The crystal structure of sulphur nitride has been determined by *X*-ray analysis. The monoclinic cell contains four molecules S_4N_4, each consisting of a distorted tetrahedron of sulphur atoms with nitrogen atoms along four edges. The distance between sulphur atoms not joined through nitrogen is 2·58 Å which is much shorter than the normal van der Waals separation. Resonance formulæ are suggested to account for this short S–S distance.

SULPHUR NITRIDE is one of the few relatively simple inorganic compounds whose molecular structure has not been determined with certainty. The molecular formula S_4N_4 is known from cryoscopic measurements, but neither methods of preparation nor properties provide conclusive evidence for its structure. Early formulations by Schenck (*Annalen*, 1896, **290**, 171), Muthmann and Clever (*Z. anorg. Chem.*, 1896, **13**, 200), Ruff and Geisel (*Ber.*, 1904, **37**, 1573), and Meuwsen and Holch (*Ber.*, 1931, **64**,2 301) were directed primarily to satisfying the then-accepted valencies of the constituent atoms, and led to assemblages of three- and four-membered rings which are inherently improbable, *e.g.*, Ruff and Geisel's formula (I).

Jaeger and Zanstra (*Proc. K. Akad. Wetensch. Amsterdam*, 1931, **34**, 782), as a result of an *X*-ray investigation, published structure (II), consisting of two interpenetrating bisphenoids of nitrogen and sulphur, which required an improbably short N–S distance of 1·2 Å, compared with 1·54 Å and 1·74 Å for double and single bonds respectively, calculated from known atomic radii. Further doubt is cast upon this work since the crystals are



(I)

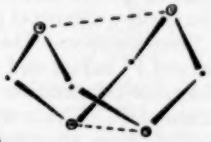


(III)

(V)

(II)

⊖ Sulphur • Nitrogen



(IV)

treated as orthorhombic, whereas their true symmetry is monoclinic. Buerger (*Amer. Min.*, 1936, **21**, 575) published a unit-cell and space-group determination, $a = 8{\cdot}74$, $b = 7{\cdot}14$, $c = 8{\cdot}64$ Å, $\beta = 87°\ 39'$, space group $P2_1/n$ containing four molecules of S_4N_4 per unit cell, but no account of further structure work is given. Arnold, Hugill, and Hutson (*J.*, 1936, 1645) proposed configuration (III), consisting of two fused five-membered rings involving resonance among several different bond structures. Chia-Si Lu and Donohue (*J. Amer. Chem. Soc.*, 1944, **66**, 818) investigated the vapour by electron diffraction (the substance

sublimes easily below 100° *in vacuo*) and were led to a configuration consisting of a bisphenoid of sulphur atoms with nitrogen atoms along four edges in square configuration (IV). They suggested resonance forms such as (V) to account for the short S–S distances across the two opposite edges of the bisphenoid not occupied by nitrogen atoms.

X-Ray Measurements and Space-group Determination.—The specimen was prepared by the action of ammonia on sulphur dichloride in an inert solvent, according to the method of Arnold, Hugill, and Hutson (*loc. cit.*). After crystallisation from carbon tetrachloride the substance formed needles elongated along the *b* axis, all of which were twinned. After recrystallisation by slow evaporation of the solvent at room temperature, a few untwinned crystals were obtained suitable for *X*-ray analysis.

Complete sets of overlapping, 15° oscillation photographs were taken about each of the three principal axes, filtered copper radiation being used. Intensities were estimated visually from a calibrated scale of intensities, additional short-exposure photographs being taken where necessary to obtain the intensities of outstandingly strong reflections. Polarisation and Lorentz corrections were applied in the usual way, giving a series of F^2 values on an arbitrary scale. No correction was made for absorption.

FIG. 1. *Patterson projection on* (010).

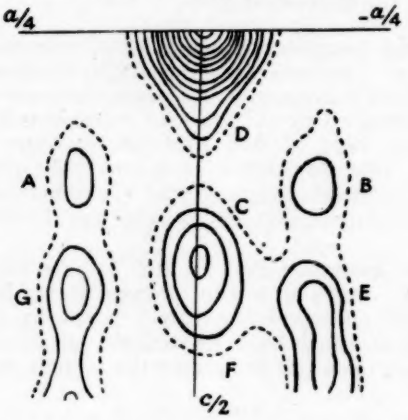
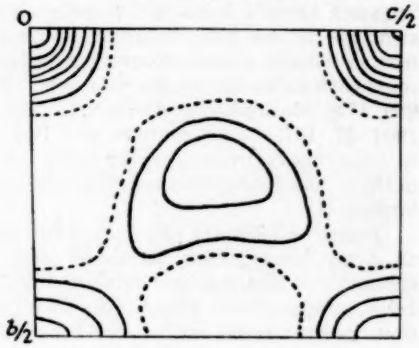


FIG. 2. *Patterson projection on* (100).



The orientation originally proposed by Buerger (*loc. cit.*), which gives an almost tetragonal cell, being retained, the following dimensions for the monoclinic unit cell were obtained: $a = 8{\cdot}75$, $b = 7{\cdot}16$, $c = 8{\cdot}65$ Å, $\beta = 87\frac{1}{2}°$, in very good agreement with those of Buerger. The space-group $P2_1/n$ was confirmed. The general position is fourfold—$\pm(x, y, z)$; $\pm(\frac{1}{2} - x)(\frac{1}{2} + y)(\frac{1}{2} - z)$. The unit-cell from the observed density (2·20 g./c.c.) contains 16 SN, or assuming a structure of discrete S_4N_4 molecules, $4S_4N_4$, which must therefore occupy a general position in the unit cell.

Structure Determination.—The (010) and (100) Patterson projections were calculated from the observed F^2 values and proved to be relatively simple. It was found possible to extract considerable information from them even in the absence of predominantly heavy atoms in the unit cell. The intramolecular distance, sulphur to sulphur bonded through nitrogen, S–(N)–S, from electron-diffraction data (Lu and Donohue, *loc. cit.*) as well as from known atomic radii and bond angles, must be in the region 2·6—2·7 Å. Two peaks *A* and *B* in the (010) Patterson projection (Fig. 1) can provisionally be identified as this vector, with possibly two others at *C* and *D*. All other peaks represent distances considerably greater than 2·7 Å even in projection. At the same time it was noted that the structure amplitudes F_{h0l} and $F_{h0\bar{l}}$ were very nearly equal, especially for low-order reflections. The simplified structure factor for those reflections is $F_{h0l} = 4 \cos 2\pi(hx + lz)$. If $F_{h0l} = F_{h0\bar{l}}$ then for every atom at (x, z) there must be a similar atom at $(x, \bar{z})$. Since the monoclinic angle β is very close to 90°, this is equivalent to two vertical planes of

symmetry *mm* mutually at right angles in this projection, in addition to the symmetry required by the space-group. The outstanding feature of the (100) Patterson projection (Fig. 2) is the very large peak at $b = 0$, $c = \frac{1}{2}$, almost equal in height to the peak at the origin. This can be accounted for if there is a pseudo-plane of symmetry in this projection at $b = \frac{1}{4}$ in addition to the *n* glide plane.

Thus in addition to the space-group symmetry, there are, in the two projections, three planes of pseudo-symmetry mutually at right angles, some of which must be satisfied by

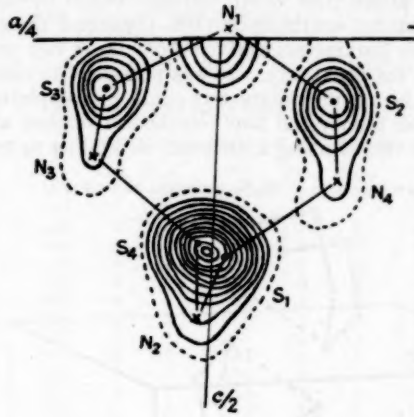
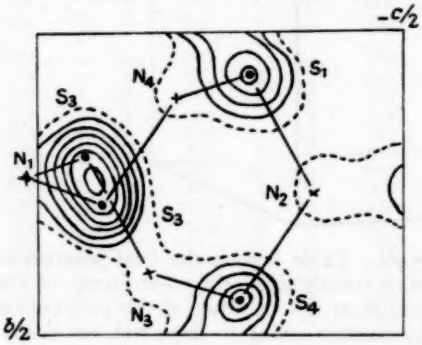
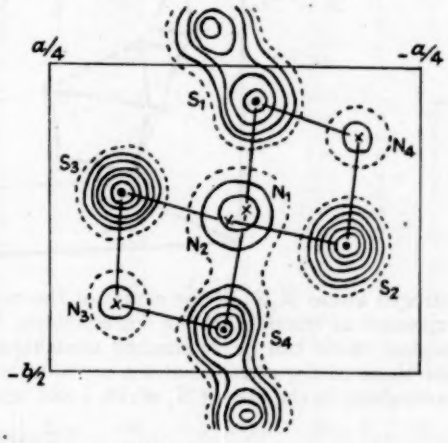


FIG. 3. *Electron density projected on* (010).

FIG. 5. *Electron density projected on* (001).

FIG. 4. *Electron density projected on* (100).

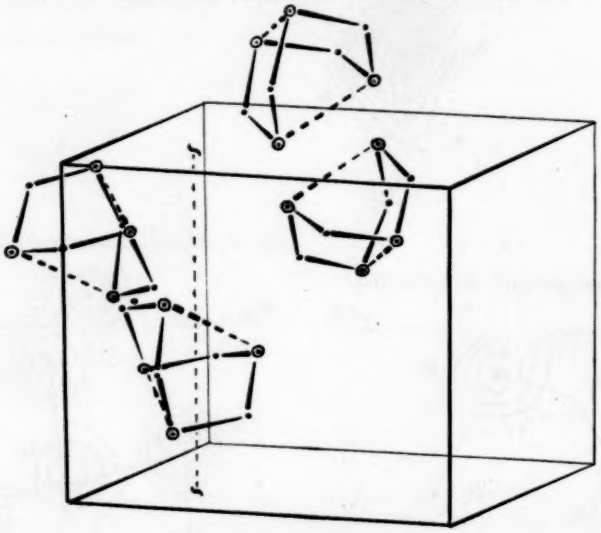




internal symmetry. Consider Lu and Donohue's tetrahedral model. If the nitrogen atoms of relatively low scattering power are neglected, we are left with an approximately tetrahedral arrangement of sulphur atoms, with six symmetry planes grouped in three pairs of mutually perpendicular planes but no centre of symmetry. Two planes of pseudo-symmetry in the unit cell can therefore be accommodated by symmetry planes of the tetrahedron, leaving the third to be satisfied by the actual arrangement of molecules in the unit cell. Peaks *E*, *F*, and *G* of the (010) Patterson projection suggested that (001) was the symmetry plane determining the arrangement of molecules. The orientation of the sulphur tetrahedron is therefore practically fixed by the other two symmetry planes, leaving *z* co-ordinates only to be determined by peaks *E*, *F*, and *G*. It was at once apparent that the resulting arrangement was very reasonable spatially and, at the same time, gave

encouraging agreement between observed and calculated structure factors for low-angle reflections. Two alternative positions were left for the nitrogen atoms, of which the more likely, from considerations of available space, was characterised by two overlapping nitrogen atoms at the origin in the (010) projection. The signs of all the structure factors F_{h0l} were computed, only the four sulphur atoms being taken into account. A Fourier synthesis on (010) was then carried out by use of Beevers and Lipson strips. The resulting projection showed unmistakable signs of a fairly large peak at the origin, together with indications of two other nitrogen atoms (the fourth nitrogen would be masked by overlapping sulphur atoms). A preliminary synthesis on (100) confirmed the general correctness of the structure. The atomic parameters derived from these two projections were refined by successive syntheses in the usual way. It was necessary to compute all three projections (Figs. 3, 4, 5) before the atomic parameters could be completely determined. The (001) projection (Fig. 5) shows clearly the four tetrahedral sulphur atoms, together with the square of nitrogen atoms viewed along a diagonal, so leading to two overlapping

FIG. 6. *General arrangement of* $4S_4N_4$ *molecules in unit cell.*



nitrogen atoms N_1N_2 at the centre of the molecule. Table 1 gives the final parameters expressed as fractions of the corresponding lattice translations—the co-ordinates of the sulphur atoms can be determined unambiguously from one or other of the projections, but those of the nitrogen atoms are a little less certain owing to imperfect resolution, particularly in the case of N_1 which is not completely resolved in any projection.

TABLE 1.

Atom	x	y	z	Atom	x	y	z
S_1	0·984	0·932	0·296	N_1	0·995	0·763	0·980
S_2	0·849	0·711	0·087	N_2	0·010	0·739	0·383
S_3	0·148	0·800	0·067	N_3	0·167	0·610	0·160
S_4	0·029	0·555	0·276	N_4	0·840	0·893	0·193

Calculated F values were obtained by using these co-ordinates and scattering factors taken from " International Tables for the Determination of Crystal Structure; " $F_{obs.}$ and $F_{calc.}$ were put on the same scale, and $F_{calc.}$ corrected by a temperature factor with $B = 4{\cdot}0$. Table 2 shows the agreement between observed and calculated values, the discrepancy calculated using the conventional expression $100\ \Sigma(F_{obs.} - F_{calc.})/\Sigma F_{obs.}$ being 20%.

Discussion of the Structure.—The molecular structure fully confirms that proposed by Lu and Donohue (*loc. cit.*), from electron-diffraction data, the bond lengths and angles being as follows:

	Electron diffraction	Crystal structure
S–N, Å	1·62	1·60
>N bond angle	112°	115°
>S bond angle	106°	102°

The four sulphur atoms (Fig. 6) form a slightly distorted tetrahedron, the pairs of sulphur atoms linked through nitrogen being separated by 2·71 Å compared with 2·58 Å for unbonded pairs (Lu and Donohue give *ca.* 2·70 Å for both these distances). Within experimental error the nitrogen atoms lie at the corners of a square. All sulphur–nitrogen

TABLE 2. *Observed and calculated structure factors for the principal zones*

(in approximate order of increasing sin θ).

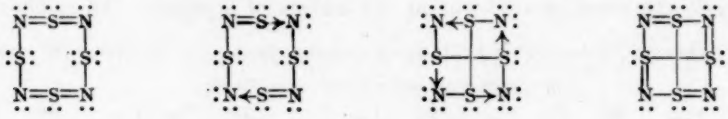
*h*0*l*	$F_{obs.}$	$F_{calc.}$	*h*0*l*	$F_{obs.}$	$F_{calc.}$	*h*0*l*	$F_{obs.}$	$F_{calc.}$	*h*0*l*	$F_{obs.}$	$F_{calc.}$	*h*0*l*	$F_{obs.}$	$F_{calc.}$
101	12	12	50$\bar{1}$	5	3	107	1	1	70$\bar{5}$	3	4	608	2	3
10$\bar{1}$	11	12	105	12	13	10$\bar{7}$	6	5	507	7	8	60$\bar{8}$	2	2
200	22	22	10$\bar{5}$	8	10	604	1	1	50$\bar{7}$	0	0	10·00	4	3
002	10	9	404	6	9	60$\bar{4}$	1	1	804	0	0	00·10	2	2
202	12	13	40$\bar{4}$	6	9	406	7	6	80$\bar{4}$	1	1	905	0	1
20$\bar{2}$	15	17	503	8	8	40$\bar{6}$	2	3	408	0	4	90$\bar{5}$	2	2
301	22	25	50$\bar{3}$	4	4	703	4	4	40$\bar{8}$	0	2	509	1	1
30$\bar{1}$	19	20	305	2	3	70$\bar{3}$	2	3	901	3	4	50$\bar{9}$	1	2
103	21	15	30$\bar{5}$	2	2	307	10	12	90$\bar{1}$	3	2	10·02	1	1
10$\bar{3}$	20	18	600	28	22	30$\bar{7}$	10	11	109	4	6	10·0$\bar{2}$	1	1
400	2	2	006	8	7	800	5	5	10$\bar{9}$	2	3	20·10	2	2
004	1	2	602	0	1	008	4	5	903	2	3	20·1$\bar{0}$	0	1
303	18	18	60$\bar{2}$	0	2	802	2	1	90$\bar{3}$	2	2	10·04	1	1
30$\bar{3}$	18	16	206	0	0	80$\bar{2}$	0	0	309	2	2	10·0$\bar{4}$	1	1
402	10	12	20$\bar{6}$	3	3	208	2	2	30$\bar{9}$	0	0	40·10	1	2
40$\bar{2}$	13	14	505	2	3	20$\bar{8}$	4	5	707	1	0	40·1$\bar{0}$	1	1
204	6	8	50$\bar{5}$	2	3	606	0	2	70$\bar{7}$	2	3	808	3	2
20$\bar{4}$	11	13	701	5	5	60$\bar{6}$	4	3	806	2	2	907	3	2
501	6	5	70$\bar{1}$	9	8	705	6	6	80$\bar{6}$	0	0	709	1	3

*hk*0	$F_{obs.}$	$F_{calc.}$	*hk*0	$F_{obs.}$	$F_{calc.}$	*hk*0	$F_{obs.}$	$F_{calc.}$	*hk*0	$F_{obs.}$	$F_{calc.}$	*hk*0	$F_{obs.}$	$F_{calc.}$
110	0	0	240	3	4	060	7	7	830	0	1	280	1	2
200	22	22	510	1	1	450	2	2	270	1	1	380	0	1
210	1	1	430	0	0	160	7	6	560	9	9	760	0	1
020	12	11	520	8	8	720	5	4	370	0	1	850	0	0
120	1	1	340	8	8	260	5	6	910	2	2	940	6	5
220	10	10	600	28	22	640	2	2	750	1	1	10·20	4	2
310	0	0	610	1	1	800	5	5	840	0	2	670	0	0
130	3	2	530	0	0	360	0	0	920	1	1	480	0	1
320	1	2	150	2	2	550	1	1	470	0	0	10·30	0	0
400	2	2	440	1	1	730	0	0	660	3	3	580	2	1
230	2	2	250	1	1	810	0	1	080	4	4	860	1	1
410	1	1	620	6	4	820	1	1	180	2	2	950	0	1
420	12	13	350	2	2	460	4	4	930	0	0	10·40	1	1
330	0	0	540	4	3	650	1	2	570	0	0			
040	6	6	630	1	1	740	5	6	10·00	4	3			
140	14	13	710	4	2	170	0	0	10·10	0	0			

0*kl*	$F_{obs.}$	$F_{calc.}$	0*kl*	$F_{obs.}$	$F_{calc.}$	0*kl*	$F_{obs.}$	$F_{calc.}$	0*kl*	$F_{obs.}$	$F_{calc.}$	0*kl*	$F_{obs.}$	$F_{calc.}$
011	1	0	041	0	1	036	6	7	056	4	4	039	1	1
002	10	9	042	8	7	017	2	2	047	0	0	075	0	0
012	12	13	015	0	0	060	7	7	071	0	0	00·10	2	2
020	12	11	034	0	1	054	4	6	038	5	6	01·10	2	4
021	1	1	025	2	2	061	3	2	072	0	0	082	0	1
022	30	27	043	0	1	027	4	4	065	0	0	083	0	1
013	4	4	006	8	7	062	2	4	073	1	1	067	1	2
031	1	2	016	0	0	046	4	4	019	0	1	058	1	2
023	1	1	035	0	1	008	4	5	057	0	0	049	1	3
004	1	2	051	2	2	063	0	1	048	0	1	076	0	1
032	8	8	044	0	1	055	2	2	029	0	2	084	0	1
014	15	14	052	1	4	037	0	0	074	2	3	085	0	1
024	11	11	026	4	5	018	1	2	066	0	1	068	0	0
033	3	2	053	0	0	028	0	1	080	4	4	059	1	1
040	6	6	045	3	4	064	0	2	081	0	0			

distances are equal, and the bond length 1·60 Å may be compared with 1·57 Å for S–N in the sulphamate ion $[SO_3{\cdot}NH_2]'$ (Brown and Cox, *J.*, 1940, 1) and 1·63 Å in the dinitrosulphite ion $SO_3{\cdot}N{<}^{NO}_{O}$ (Cox, Jeffrey, and Stadler, *J.*, 1949, 1783).

One point of interest in the molecule is the short distance between pairs of sulphur atoms not linked through nitrogen. The observed value is 2·58 Å compared with 3·7 Å for the normal van der Waals separation and 2·1 Å for an ordinary single bond. This was explained by Lu and Donohue on the basis of resonance forms, some of which contain a single bond between these two atoms, *e.g.*,



(VI) (VII) (VIII) (IX)

Of these, (VI) is probably the most important, containing sulphur with a decet of electrons, but the importance of the cross-bonded structures is shown by the short S–S distances across the other two sides of the tetrahedron. It should be noted that the observed distance is only about 0·1 Å shorter than the separation of sulphur atoms linked through nitrogen, where they are forced together by the fixed N–S distances and bond angles. Purely geometrical considerations may therefore play a part, although cross-bonded structures confer some additional stability to account for the existence of the present structure rather than of other forms of puckered ring containing similar bond lengths and angles. The angle between this third " bond " and the other two bonds formed by the sulphur atom is approximately 90°.

The packing of the molecules in the unit cell (Fig. 6) is purely molecular, as already indicated by the low melting point and the volatility of the crystals. The distances of closest approach of neighbouring molecules are S–N 3·3 Å and S–S 3·7 Å, in good agreement with the accepted van der Waals radii of these atoms. The abundant formation of twin crystals follows from the pseudo-symmetry of the unit cell and the closeness of the monoclinic angle to 90°.

The author thanks Mr. W. Press for assistance with the calculations.

Imperial Chemical Industries Limited, Research Department,
Billingham, Co. Durham. [*Received, April 5th*, 1951.]

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298. *Pteridine Studies. Part II.* 6- and 7-Hydroxypteridines and their Derivatives.*

By Adrien Albert, D. J. Brown, and Gordon Cheeseman.

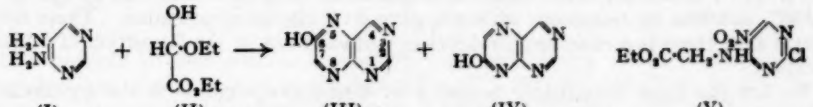
Syntheses of a number of monosubstituted pteridines and dihydropteridines are reported, together with their ionization constants, R_F values, and ultra-violet spectra. All possible mono-hydroxypteridines are now known: the 6-isomeride is distinguished by giving a hysteresis loop when titrated, which is ascribed to a slow tautomerism.

The syntheses of monosubstituted pteridines, commenced in Part I,* have been continued by the introduction of various groups in the 6-position and of the hydroxy-group in the 7-position.

When 4 : 5-diaminopyrimidine (I) was heated with ethyl glyoxylate hemiacetal (II) in water at 100°, two isomeric monohydroxypteridines were obtained. The less basic isomeride, which predominated (65% yield) when the reaction was carried out at pH 6,

* Part I, *J.*, 1951, 474.

was separated from the more basic isomeride (25% yield) at pH 2 and freed from traces of the latter by recrystallization, as the sodium salt, from boiling N-sodium hydroxide. The more basic isomeride, which predominated when the reaction was carried out at pH −0·2 was freed from the less basic isomeride (20% yield) by filtration at pH 2 and was liberated in 65% yield when the pH was raised to 5·5. It proved to be rapidly destroyed by boiling N-sodium hydroxide.



(I) (II) (III) (IV) (V)

In the synthesis of more complex pteridines, highly acid conditions favour the hydroxy-group entering the 6-position, and less acid conditions may direct it to the 7-position (Purrmann, *Annalen*, 1941, **548**, 284; Elion, Hitchings, and Russell, *J. Amer. Chem. Soc.*, 1950, **72**, 78). Hence the less and the more basic isomeride produced in the above reaction should be 7- and 6-hydroxypteridine, respectively. This was confirmed by the synthesis of 6-hydroxypteridine (III) by an unambiguous method, *viz.*, the oxidation of 7 : 8-dihydro-6-hydroxypteridine, prepared by the reduction, ring closure, and dehalogenation of 4-carbethoxymethylamino-2-chloro-5-nitropyrimidine (V) (Boon, Jones, and Ramage, *J.*, 1951, 96). The preceding route, however, gave a better yield as well as a small amount of (IV) as a valuable by-product.

6-*Hydroxypteridine and its Derivatives.*—When 6-hydroxypteridine was gently warmed with sodium amalgam, 85% of 7 : 8-dihydro-6-hydroxypteridine was obtained. It was similarly obtained from 6 : 7-dihydroxypteridine (made by heating 4 : 5-diaminopyrimidine with oxalic acid). The identity of the specimens of 7 : 8-dihydro-6-hydroxypteridine prepared by these three routes was confirmed by measurements of solubility, ionization constants, ultra-violet and infra-red spectroscopy, and by paper chromatography in four different solvents. This reduction of 6 : 7-dihydroxypteridine is analogous to the transformation of leucopterin (2-amino-4 : 6 : 7-trihydroxypteridine) to dihydroxanthopterin (2-amino-7 : 8-dihydro-4 : 6-dihydroxypteridine) under similar conditions (Totter, *J. Biol. Chem.*, 1944, **154**, 105; Boon and Leigh, *J.*, 1951, 1497).

All three specimens of 7 : 8-dihydro-6-hydroxypteridine gave 6-hydroxypteridine by oxidation with potassium permanganate. Thus no analogue has been produced of the so-called β-form of dihydroxanthopterin, which resists oxidation to xanthopterin by this reagent (Hitchings and Elion, *J. Amer. Chem. Soc.*, 1949, **71**, 467).

6-Hydroxypterdine differed from 2-, 4-, and 7-hydroxypteridines in resisting destruction of the pteridinei ring by phosphorus halides. Phosphorus oxychloride alone had no effect on 6-hydroxypteridine but, in combination with phosphorus pentachloride, produced 6-chloropteridine. 6-Chloropteridine was converted into 6-amino-, 6-dimethylamino- and 6-methoxy-pteridines in the usual way. The spectra of 6-amino- and 6-dimethylamino-pteridines are given in Fig. 5 (p. 1626). As with the pair aniline–dimethylaniline, the tertiary amine absorbs at longer wave-lengths. However, the two spectra are so similar as to suggest that 6-aminopteridine cannot have the isomeric "imino"-structure. 6-Amino- and 6-dimethylamino-pteridines, more sensitive to acids than their 2- and 4-isomerides, are fairly rapidly hydrolysed to 6-hydroxypteridine at pH 2 (20°). As with the other amino-pteridines, the cations absorb at much lower wave-lengths than the neutral molecules.

Profound decomposition took place when the preparation of 6-mercaptopteridine was attempted by the reaction of 6-chloropteridine with thiourea or sodium hydrogen sulphide, or by the reaction of 6-hydroxypteridine with phosphorus pentasulphide.

6-Hydroxypteridine gave no colour with diazotized amines (aniline, *p*-aminodimethylaniline, and 2 : 5-dichloroaniline) under the conditions which were said to give an orange-brown colour from the last-named and xanthopterin (Schöpf and Becker, *Annalen*, 1933, **507**, 266). Xanthopterin had not been obtained pure in 1933, but pure xanthopterin (prepared by the method of Elion, Light, and Hitchings, *J. Amer. Chem. Soc.*, 1949, **71**, 741) gave no decisive colour change. 6-Hydroxypteridine could not be benzoylated.

6-Hydroxypteridine was oxidized to 6 : 7-dihydroxypteridine by hydrogen peroxide; by this method xanthopterin had been oxidized to leucopterin (Wieland and Purrmann, *Annalen*, 1939, **539**, 179), but in that case the 7-position was the only one open to substitution. The same authors (*Annalen*, 1940, **544**, 163) converted xanthopterin into leucopterin by shaking a suspension in dilute acetic acid with oxygen in the presence of Adams's platinum catalyst; however we found 6-hydroxypteridine unaltered by this treatment, even at 100°, when completely dissolved in glacial acetic acid. Sodamide in diethylaniline at 150°, followed by treatment with ice, gave 6 : 7-dihydroxypteridine. These reactions suggest that there is a considerable deficiency of electrons in the 7-position of 6-hydroxypteridine.

By far the most remarkable property of 6-hydroxypteridine is the hysteresis loop which is produced on titration (Fig. 1). Running alkali into an aqueous solution of 6-hydroxypteridine gave pH values which are much higher than those found on back-titration with acid. Moreover, the pH tends to fall during a pause in the addition of alkali and to rise during the addition of acid, equilibrium being obtained in approximately 2 hours (the loop was retraced when the solution was re-titrated). On the other hand, the basic group of this substance can be titrated, and back-titrated, without suggestion of abnormality (Fig. 1).

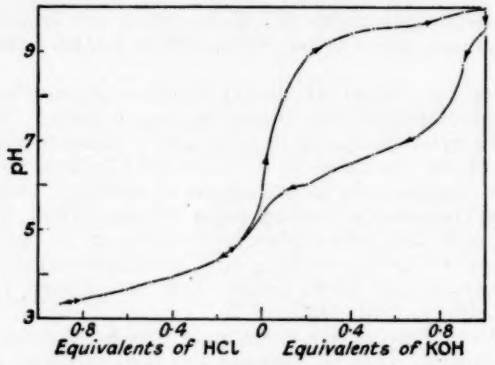


FIG. 1. *Hysteresis loop produced on titrating 250 ml. of 0·002M-aqueous 6-hydroxypteridine with 1 equiv. (5 ml.) of 0·1N-acid and -alkali at 20°.*

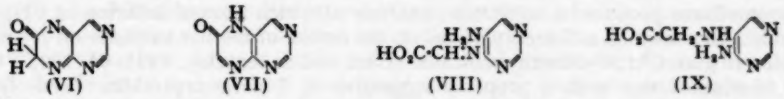
It has been suggested, on spectrographic grounds, that xanthopterin (2-amino-4 : 6-dihydroxypteridine) undergoes slow tautomerism in alkaline solution (Schou, *Arch. Biochem.*, 1950, **28**, 10). We found that a potentiometric back-titration produced pH drifts as with 6-hydroxypteridine. This effect in xanthopterin must be ascribed to the 6-hydroxy-group because neither 2-amino- nor 4-hydroxy-pteridine forms hysteresis loops upon titration; in fact we never observed this phenomenon in any hydroxy-heterocyclic substance that was not a derivative of 6-hydroxypteridine : even such closely related substances as 2-hydroxypyrazine * and 2-hydroxyquinoxaline * did not behave in this way.

It is not easy to decide whether this effect involves a change from (III) to (VI) or to (VII). Of these two types of tautomerism, prototropy between carbon and oxygen is commonly slow enough to be detected by physical means. On the other hand, prototropy between nitrogen and oxygen is usually considered to be instantaneous, although the independent existence of both ketimine and enamine tautomers of the neutral molecules of 2- and 4-hydroxyacridines has been demonstrated spectroscopically (Albert and Short, *J.*, 1945, 760).

That (VI) may be involved is suggested by two pieces of evidence. First, 7 : 8-dihydro-6-hydroxypteridine does not give this effect and could not do so because it cannot take another hydrogen in the 7-position. 6 : 7-Dihydroxypteridine also does not give the effect, and this may be attributed partly to steric hindrance by the 7-hydroxy-group and par-

* pK_a 8·23 ± 0·02 and 9·08 ± 0·03 respectively at 20°.

ticularly to the well-known favouring of enolization by electron-attracting substituents [Meyer, *Ber.*, 1912, **45**, 2843; a hydroxy-group would be electron-attracting in the 7-position of (VI)]. However, this is only negative evidence and, if structure (VI) were involved, it



should be possible to demonstrate a reactive methylene group in the 7-position of 6-hydroxypteridine, similar to that in the 5-position of barbituric acid (2 : 4 : 6-trihydroxypyrimidine). However, unlike barbituric acid, 6-hydroxypteridine could not be nitrated, with or without the addition of sulphuric or acetic acid; neither could it be nitrosated, brominated, or caused to react with aldehydes. Moreover barbituric acid did not show slow tautomerism on potentiometric titration.

It is unlikely that the slow tautomerism involves ring fission by alkali to the pyrimidine (VIII). The ultra-violet spectrum of the 6-hydroxypteridine anion (Fig. 2) became steady

FIG. 2. *6-Hydroxypteridine (absorption spectra in water).*

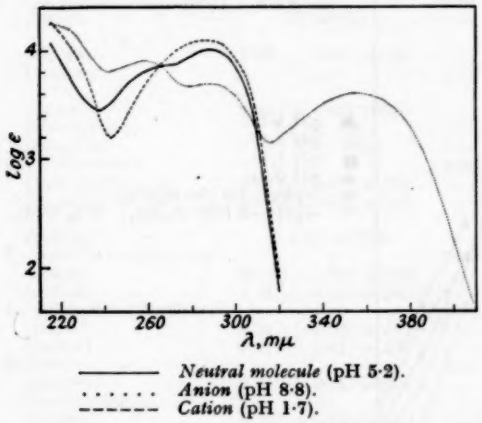
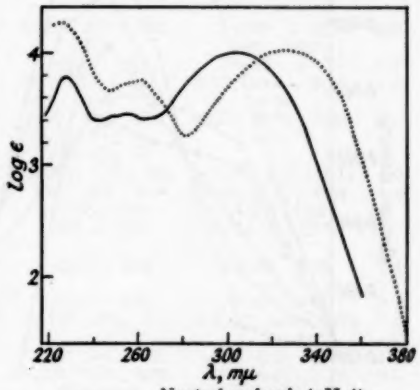


FIG. 3. *7-Hydroxypteridine (absorption spectra in water).*



n 2 hours at pH 8·8 and remained so for at least 8 hours; it was similar in outline to the anionic spectra of 2- and 7-hydroxypteridine and the long-wave peak of the 6-isomeride fell between those of these isomerides (cf. Figs. 2, 3, and Part I). Moreover, it overlaps much of the spectrum of 6-aminopteridine (neutral molecule), a relation to be expected from the comparable behaviour of the 2- and 4-hydroxy- and -amino-isomerides (see Part I). The spectrum of the neutral molecule of 6-hydroxypteridine (stable for 48 hours at pH 5·2) is similar in shape to that of the 2-isomeride but shifted a little to shorter wavelengths.

Furthermore, the infra-red spectra of 6-hydroxypteridine and its sodium salt (as solids) closely resembled one another in the 1400—1700-cm.$^{-1}$ region. Had the ring opened to give (VIII), bands characteristic of NH_2, C=N, and pyrimidine-ring absorption should have appeared in this region. The intensity of the band at 1700 cm.$^{-1}$, which is almost certainly a carbonyl bond-stretching vibration, was very much reduced after salt formation, as would be expected.

6-Amino- and 6-dimethylamino-pteridines showed no hysteresis on titration.

7-Hydroxypteridine and its Derivatives.—These were outstanding among pteridines for their ready tendency to crystallize quickly and in large crystals.

7-Hydroxypteridine was broken down by phosphorus oxychloride, pentachloride, or

pentasulphide; hence 7-chloro- and 7-mercapto-pteridines could not be obtained in this way. 7-Hydroxypteridine was unaffected by ammonia in *p*-cresol at 200°.

Methylation of 7-hydroxypteridine by diazomethane in ether gave an *N*-methyl-7-pteridone. The spectrum (Table 1) resembles that of 7-hydroxypteridine. An excess of diazomethane produced a substance, analysis of which showed addition of CH_2 to the molecule; this may be a *C*-methylation, cf. the action of methyl sulphate on N^9-methylxanthine to give C^8 : N^9-dimethylxanthine (Biltz and Sauer, *Ber.*, 1931, **64**, 752). Only a trace of a substance with a property suggestive of 7-methoxypteridine (hydrolysis by boiling with N-sodium hydroxide for 1 minute, as with the 2-, 4-, and 6-isomers) could be obtained by alkylation under various conditions.

When 7-hydroxypteridine was hydrogenated over platinum in 0·1N-sodium hydroxide or boiled with alkaline sodium dithionite (hydrosulphite), an amphoteric white substance,

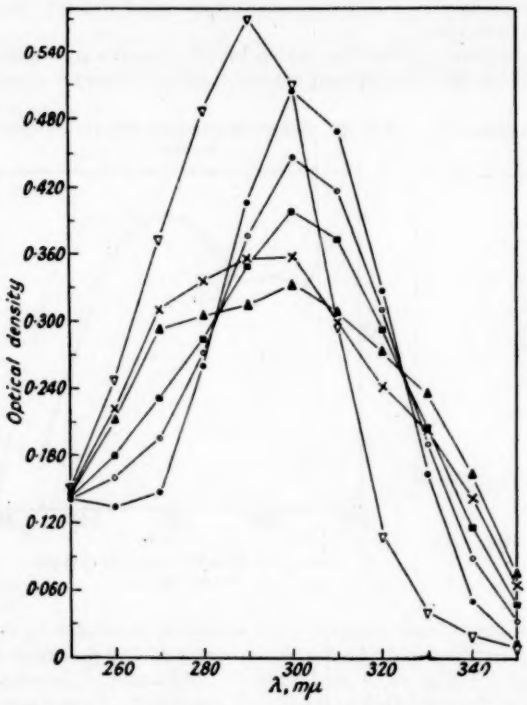


FIG. 4. *7-Hydroxypteridine (optical density of* $5·0 \times 10^{-5}$M*-aqueous solution).*

$C_6H_8O_2N_4$, was isolated on acidification to pH 5 at, or below, 20°. Acidification at a higher temperature gave also a dihydro-7-hydroxypteridine ($C_6H_6ON_4$). The H_8 substance could be completely converted by refluxing N-hydrochloric acid during 1 hour into the H_6 substance and then regenerated by boiling N-sodium hydroxide in one minute. These reactions, and the fact that the two substances differ from one another by the elements of water, suggested that ring-opening and -closing were involved. That the H_8 substance was a carboxylic acid was confirmed by its ready esterification in methanolic hydrogen chloride. The strikingly different R_F values of these three substances in paper chromatography made it easy to follow these reactions.

In the case of the dihydro-7-hydroxypteridine, reduction is assumed to have taken place exclusively in the pyrazine ring because pyrazines are readily hydrogenated under alkaline conditions (Krems and Spoerri, *Chem. Reviews*, 1947, **40**, 279), but pyrimidines only with difficulty (Lythgoe and Rayner, *J.*, 1951, 2323; Brown and Johnson, *J. Amer. Chem. Soc.*, 1923, **45**, 2702). Moreover, all known reductions in the pteridine series have occurred

exclusively at the pyrazine ring, *e.g.*, 6-hydroxypteridine and leucopterin (see above), folic acid (Pohland, Flynn, Jones, and Shive, *J. Amer. Chem. Soc.*, 1951, **73**, 3248), and 2-ethoxy-4-methyl-6 : 7-diphenylpteridine (Polonovski, Pesson, and Pinster, *Compt. rend.*, 1950, **230**, 2205).

The dihydro-7-hydroxypteridine is amphoteric (Table 1) and hence could not be the 7 : 8-dihydro-derivative which would not be acidic. Again, its $\lambda_{max.}$ value exceeds that of 7-hydroxypteridine and hence it could not be the 5 : 8-dihydro-derivative which has an isolated double bond and a short conjugated pathway. Hence it is considered to be 5 : 6-dihydro-7-hydroxypteridine. It was oxidized to 7-hydroxypteridine by potassium permanganate. The carboxylic acid, which would accordingly be 4-amino-5-carboxymethylaminopyrimidine (IX), was destroyed when oxidation was attempted under the same conditions.

Nitrous acid destroyed 7-hydroxypteridine, under the conditions which enabled Wieland and Liebig to insert a 6-hydroxyl-group into *iso*xanthopterin (2-amino-4 : 7-dihydroxy-

TABLE 1. *Physical properties of pteridines.*

Pteridine derivative	pK_a (in water) and concn. at which determined (20°)	R_F [2]	Spectrography in water: $\lambda_{max.}$ (mμ)	log $\varepsilon_{max.}$ (mol.)	pH
6-Hydroxy (+1H_2O)	—	0·30—0·70 [3]	<215; 289	>4·10; 4·00	5·2
(anion)	6·7 M/500	—	<215; 258; 289; 356	>4·25; 3·90; 3·69; 3·60	8·8
(cation)	3·67 (± 0·04) M/500	—	<215; 287	>4·27; 4·09	1·7
7-Hydroxy	—	0·75 [4]	227; 248 + 256 [5]; 303	3·79; 3·44 + 3·45; 4·00	4·0
(anion)	6·41 (± 0·02) M/200	—	226; 260; 326	4·27; 3·76; 4·04	9·0
(monocation)	1·2 (± 0·2) [1]	—	(See Fig. 4)	—	—
(dication)	−2·0 (± 0·5) [1]	—	(See Fig. 4)	—	—
6 : 7-Dihydroxy	—	0·35 [5]	<220; 249; 301	>3·98; 3·71; 4·18	4·0
(monoanion)	6·87 (± 0·03) M/500	—	227; 268; 319	4·03; 3·71; 4·29	8·4
(dianion)	10·0 (± 0·08) M/500	—	<220; 240; 324 + 338	>4·47; 4·13; 4·30 + 4·25	12
(cation)	<2·7 M/500	—	—	—	—
7 : 8-Dihydro-6-hydroxy	—	0·50 [6]	<215; 293	>4·09; 3·94	7·4
(anion)	10·54 (± 0·02) M/500	—	—	—	—
(cation)	4·78 (± 0·03) M/500	—	<210; 292	>4·20; 4·01	2·4
5 : 6-Dihydro-7-hydroxy	—	0·75 [7]	<215; 271; 319	>4·42; 3·58; 3·70	6·0
(anion)	9·94 (± 0·05) M/400	—	—	—	—
(cation)	3·36 (± 0·01) M/400	—	223; 284; 352	4·47; 3·74; 3·71	1·02
6-Amino	—	0·50	223; 258; 362	4·30; 4·01; 3·75	7·0
(cation)	4·15 (± 0·02) M/200	—	(See text)	—	
6-Dimethylamino	—	—	231; 279; 399	4·21; 4·17; 3·74	7·0
(cation)	4·31 (± 0·03) M/200	—	(See text)	—	—
6-Chloro	—	—	(220; 303 + 310 + 315 [9]) [10]	4·46; 3·84 + 3·92 + 3·86	—
6-Methoxy	—	—	(<215; 303 + 309 + 316 + 323 + 331 [9]) [10]	>4·36; 3·83 + 3·84 + 4·01 + 3·84 + 3·97	—
(cation)	3·60 (± 0·03) M/100	—	—	—	—
(*N*-Methyl-7-pteridone)	—	—	<220; 250 + 257; 306	>4·13; 3·55 + 3·54 3·97	4·0
(cation)	1·1 (± 0·1) M/30	—	<220; 295	>4·19; 3·97	−2·0
(4-Amino-5-carboxymethylaminopyrimidine)	—	0·30 [6]	<220; 282	>4·04; 3·93	4·84
(anion)	3·02 (± 0·03) M/100	—	—	—	—
(cation)	6·67 (± 0·02) M/100	—	<220; 288	>4·05; 3·94	1·04

[1] Determined spectroscopically. [2] In butanol–acetic acid, 4-aminopteridine (R_F = 0·70) and 4-hydroxypteridine (R_F = 0·50) being run as controls. [3] Long streak, because of slow tautomerism in this solvent, but a well-resolved spot (R_F 0·90) is given in a mixture of 9 parts of dimethylformamide (azeotrope containing 6% of formic acid) and 1 part of water. [4] This spot is invisible under Wood's light (360 mμ) unless the paper has been exposed to strong daylight; a dark spot is given under light of 254 mμ which changes to bright blue after 1 minute's irradiation and is then bright violet under Wood's light (photo-oxidation effect). [5] Bright violet spot. [6] Dark spot. [7] Bright violet spot under Wood's light without prior irradiation. [8] Not completely resolved. [9] Fine structure. [10] In *cyclo*hexane because of ready hydrolysis by water; pteridine gives almost the same spectrum in both solvents.

pteridine) (*Annalen*, 1944, **555**, 146). However, cold brown nitric acid (*d* 1·5) converted 7-hydroxypteridine into 6 : 7-dihydroxypteridine, thus providing yet a third synthesis of this new compound. Hydrogen peroxide (used as in the oxidation of 6-hydroxypteridine) produced only a trace of the dihydroxy-compound; the latter was identified as a product of the action of diffuse sunlight and of ultra-violet light (principally λ 254 mμ) on 7-hydroxypteridine.

7-Hydroxypteridine could not be benzoylated. Both 6- and 7-hydroxypteridine were reduced by cold hydriodic acid (*d* 1·94 or 1·7). The colour of the liberated iodine persisted to the same extent after dilution with water; in contrast, several derivatives of 7-hydroxypteridine (*e.g.*, *iso*xanthopterin) decolorize the liberated iodine on dilution although xanthopterin (a 6-hydroxypteridine) does not (Wieland, Tartter, and Purrmann, *Annalen*, 1940, **545**, 209). 7-Hydroxypteridine did not couple with diazotized 2 : 5-dichloroaniline.

The spectra of 7-hydroxypteridine given in Fig. 3 somewhat resemble those of 4-hydroxypteridine. Fig. 4 shows changes in the spectra in solutions of increasing acid

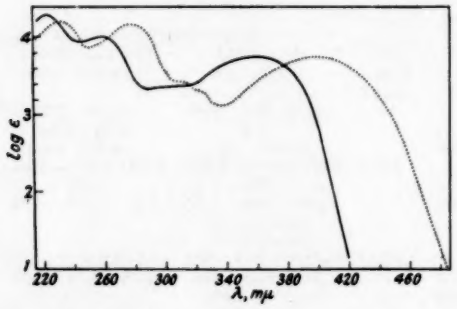


FIG. 5. *Absorption spectra in water.*

——— 6-*Aminopteridine* (*neutral molecule*, pH 7·0).
. . . . . 6-*Dimethylaminopteridine* (*neutral molecule*, pH 7·0).

strength : these changes (which are reversed when the pH is increased) reveal the formation of two cations.

Physical Constants.—A number of ionization constants are recorded in Table 1. 6- and 7-Hydroxypteridine are stronger acids than their isomerides (cf. Part I). Of all the monohydroxypteridines, only the 6-isomeride has marked basic properties.

Xanthopterin was found in Part I to have two acidic pK_a values (6·25 and 9·23) : the 6·25 value can now be definitely assigned to the 6-hydroxy-group, because of the relative strength of 6-hydroxypteridine (cf. 4-hydroxypteridine, pK_a 7·89). As would be expected, once the 6-hydroxy-group in xanthopterin has ionized, the ionization of the 4-hydroxy-group is depressed by the coulombic effect.

TABLE 2. *Fluorescences in dilute aqueous solution observed by the light of a Wood's lamp* (*principally* 360 *mμ*).

Pteridine derivative	Water	0·05N-NaOH	0·05N-H_2SO_4
4-Hydroxy (for comparison with Part I)	Violet ++	Blue +	Little or none
6-Hydroxy	None	None	None
7-Hydroxy	Violet ++	None	Little or none
6 : 7-Dihydroxy	Violet +	Little or none	Violet +
7 : 8-Dihydro-6-hydroxy	None	Violet +	None
5 : 6-Dihydro-7-hydroxy	Violet +	Violet ++	Violet ++
6-Amino	Violet ++	Violet ++	Blue ++
6-Dimethylamino	Yellow +	Yellow +	Violet +

Table 1 also summarizes the spectrographic and chromatographic data. We wish to withdraw the R_F of 0·30 recorded for pteridine in Part I as being due to photo-decomposition of this unstable substance.

The new substances described in this paper differ from xanthopterin by not fluorescing to any extent in daylight. The colours seen in ultra-violet light are given in Table 2.

Experimental

(M. p.s are uncorrected. Microanalyses were by Mr. A. Bennett and Mr. R. Baker, Beckenham.)

Physical Measurements.—The absorption spectra, potentiometric titrations, and paper chromatography were carried out as described in Part I.

In order to choose two suitable conditions of acidity to give maximal yields of 6- and 7-hydroxypteridines, the pK_a values of 4 : 5-diaminopyrimidine were determined and found to be 6·03 ± 0·04 (M/100) and <0 (M/1), both at 20°. The higher value corresponds to the ionization of 4-aminopyrimidine (pK_a, 5·71; Albert, Goldacre, and Phillips, *J.*, 1948, 2240), and the latter to that of 5-aminopyrimidine (2·83), after allowance for depression due to coulombic repulsion of the second proton after the first ionization.

Ethyl glyoxylate hemiacetal was prepared from ethyl tartrate and sodium bismuthate by Rigby's method (*J.*, 1950, 1912).

6-*Hydroxypteridine and its derivatives.*

6-*Hydroxypteridine.*—(*a*) *Direct synthesis.* 4 : 5-Diaminopyrimidine (4·4 g., 0·04 mole) was dissolved in 2N-sulphuric acid (80 ml.) at 30°. Ethyl glyoxylate hemiacetal (9 g., 0·06 mole) was added. The mixture was shaken until clear (5 minutes) and kept at about 20° for 18 hours. It was then gently refluxed for 15 minutes, clarified with carbon, and taken to pH 2·0 (metanil-yellow) with 6N-sodium hydroxide (about 16 ml.). After an hour at 20° the 7-hydroxypteridine (see below) was filtered off (20% yield). The filtrate was taken to pH 5·5 (bromocresol-green) with sodium citrate (10 g.) and 2·5N-sodium hydroxide (about 25 ml.) and chilled overnight. The white crystals were recrystallized from 230 parts of water, giving 4·3 g. (65%) of 6-*hydroxypteridine monohydrate* (Found, for material dried at 120°/0·1 mm.: C, 43·7; H, 3·45; N, 33·7. $C_6H_4ON_4,H_2O$ requires C, 43·4; H, 3·65; N, 33·75%). 6-Hydroxypteridine decomposes progressively on heating above 240°. It is soluble in 35 parts of boiling dimethylformamide (acid-free, or formic acid azeotrope) and the solution does not deposit solid at 20°. It dissolves in 50 parts of boiling acetic acid but is almost insoluble in pyridine, butanol, acetone, toluene, and light petroleum. It is decomposed by 0·1N-sodium hydroxide (almost instantaneously at 100°): the product is less soluble than 1 : 2000 in boiling water and very soluble in cold N-sodium hydroxide and appears to be a polymer. 6-Hydroxypteridine hydrochloride crystallizes from a 15% solution in hot N-hydrochloric acid. Unlike 2-hydroxypteridine, it is unchanged by 10N-hydrochloric acid at 20°.

(*b*) *From its* 7 : 8-*dihydro-derivative.* 7 : 8-Dihydro-6-hydroxypteridine (0·4 g.) was dissolved in a boiling aqueous sodium hydroxide (0·2 g. in 25 ml.) and quickly cooled to 20°. Potassium permanganate (17 ml.; 0·1M) was added during 10 minutes, with agitation. The suspension was centrifuged, the remaining solid was extracted with boiling water (12 ml.), and the combined extracts were brought to pH 5·5 and refrigerated overnight. The 6-hydroxypteridine (80% yield) was filtered off and recrystallized from water.

7 : 8-*Dihydro-6-hydroxypteridine.*—Powdered sodium amalgam (48 g., 4%) was added with gentle shaking to a suspension of 6-hydroxypteridine monohydrate (3·3 g., 0·02 mole) in water (24 ml.), at such a rate that the temperature remained between 45° and 50°. The mercury was run off. (At this stage when 6 : 7-dihydroxypteridine was the starting material, the residual solution was acidified with hydrochloric acid to pH 3·3 and kept at 20° for an hour; charcoal was then added and the mixture filtered from unchanged dihydroxypteridine.) The filtrate was adjusted to pH 8. After refrigeration overnight, the 7 : 8-dihydro-6-hydroxypteridine was filtered off and dried at 110°. It was purified by recrystallization from 400 parts of boiling water (white crystals, 85% yield). It decomposes between 310° and 340° without melting. It also recrystallizes well from (neutral) dimethylformamide and is slightly more soluble in organic solvents than 6-hydroxypteridine (Found: C, 48·0; H, 3·8; N, 37·7. Calc. for $C_6H_6ON_4$: C, 48·0; H, 4·0; N, 37·3%.) It is not oxidizable by iodine or by silver oxide (in contrast to dihydroxanthopterin, Totter, *loc. cit.*).

6 : 7-*Dihydroxypteridine. Direct Synthesis.*—Oxalic acid dihydrate (8·8 g., 7 equivs.) and 4 : 5-diaminopyrimidine (1·1 g.) were heated, under a slight vacuum (10—15 cm. of mercury), to 160° during 30 minutes and kept at 160—170° for 2 hours. The product was extracted with boiling water (125 ml.) containing enough sodium hydroxide for the mixture to give the full red colour with phenolphthalein. The filtrate was brought to pH 4 with acetic acid, cooled, and filtered after 3 hours. Recrystallization of the precipitate from 290 parts of boiling water gave large white plates of 6 : 7-*dihydroxypteridine* (1·45 g., 88%) (Found: C, 44·0; H, 2·3; N, 34·5.

$C_6H_4O_2N_4$ requires C, 43·9; H, 2·45; N, 34·2%). It is unchanged when heated to 350° or boiled with 10N-hydrochloric acid. It is almost insoluble in dilute acids and in common organic solvents, including butanol and pyridine; however it is very soluble in formamide and 4-formylmorpholine. Purification through the potassium salt was found to be as effective as recrystallization from water : 6 : 7-dihydroxypteridine (1·64 g.) and potassium carbonate (2 g., 3 equivs.) were dissolved in boiling water (32 ml.). The solution was stirred with charcoal and filtered. Next day, the potassium salt was filtered off, dissolved in boiling water (25 ml.) with the help of a little sodium hydroxide, and brought to pH 4 with acetic acid (87% recovery).

6-*Chloropteridine.*—A mixture of dried and finely ground 6-hydroxypteridine monohydrate (1 g.), phosphorus pentachloride (5 g.), and freshly distilled phosphorus oxychloride (50 ml.) was refluxed for 2 hours in a bath at 115—120°. The phosphorus oxychloride was removed by vacuum distillation at 60° and the residue was cautiously decomposed by stirring with ice, neutralized with 10N-sodium hydroxide solution, and filtered. The filtrate was exhaustively extracted with ice-cold chloroform. During the extraction the aqueous layer, which tended to become acid, was kept at pH 7. The chloroform extracts were dried (Na_2SO_4 + a little K_2CO_3), and the solvent was evaporated in a vacuum, leaving 6-*chloropteridine* (0·65 g., 65%). A smaller percentage yield was obtained when 8 g. of starting material were used. For analysis, it was crystallized from 250 parts of light petroleum (b. p. 60—80°), then from 20 parts of alcohol, giving pale yellow crystals, decomp. 146—147° (Found : Cl, 21·2. $C_6H_3N_4Cl$ requires Cl, 21·3%).

6-*Aminopteridine.*—Dry ammonia was passed into a filtered solution of crude 6-chloropteridine (0·85 g.) in benzene (85 ml.) at 20° for an hour. The precipitate was recrystallized from boiling water (80 ml.) containing carbon (0·3 g.). A further quantity was obtained from the mother-liquor. On recrystallization from water 6-*aminopteridine* was thus obtained as 1-cm. long yellow needles (53% yield) which decompose rapidly when heated above 300° and give green-fluorescing solutions (Found : C, 48·9; H, 3·4; N, 47·65. $C_6H_5N_5$ requires C, 49·0; H, 3·4; N, 47·6%). It was largely destroyed when heated under reflux with acetic anhydride for 30 minutes.

6-*Dimethylaminopteridine.*—Methanolic dimethylamine (50% w/v; 18 ml.) was added to a solution of crude 6-chloropteridine (1·5 g.) in methanol (50 ml.). After 4 hours at 20°, the solution was concentrated to *ca.* 10 ml. and treated with charcoal. The cooled filtrate deposited 6-dimethylaminopteridine in two crops, m. p. 210—211° (total yield, 78%). After dissolution in methanol (30 parts, containing charcoal), the filtrate was concentrated, to yield long yellow crystals of 6-*dimethylaminopteridine*, m. p. 212° (Found : C, 55·0; H, 4·85; N, 40·0. $C_8H_9N_5$ requires C, 54·8; H, 5·2; N, 40·0%).

6-*Methoxypteridine.*—A solution of sodium methoxide (9·2 ml., 1 equiv.), prepared from sodium (0·5 g.) and methanol (50 ml.), was added to an ice-cooled solution of crude 6-chloropteridine (0·66 g.) in methanol (25 ml.). The reaction mixture was kept at 20° for 30 minutes and then neutralized with a rapid stream of carbon dioxide. The residue obtained after removal of solvent in a vacuum was repeatedly extracted with light petroleum (b. p. 60—80°; total 300 ml.) until constant in weight. It was ground between each extraction. The combined extracts were boiled with charcoal, filtered, and concentrated to 50 ml., depositing 6-methoxypteridine in two crops (m. p. 122—125°) (total yield, 53%). Recrystallization from light petroleum (b. p. 60—80°; 120 parts) gave pure 6-*methoxypteridine* as slightly yellow needles, m. p. 124—125° (80% recovery) (Found : C, 52·1; H, 3·3; N, 34·3. $C_7H_6ON_4$ requires C, 51·85; H, 3·7; N, 34·55%).

Oxidation of 6-*Hydroxypteridine to* 6 : 7-*Dihydroxypteridine.*—6-Hydroxypteridine monohydrate (1 g.) was dissolved in boiling acetic acid (50 ml.). Hydrogen peroxide (15 ml.; 30%) was added and the mixture kept at 20° for 3 days. The precipitate was filtered off, ground under hydrogen peroxide (20 ml.; 30%), and kept at 20° for 4 days. The crystals were filtered off and boiled with water (50 ml.). The suspension was taken to pH 2·0 (metanil-yellow) with sulphuric acid and refrigerated. The crystals which were deposited were recrystallized from water, giving 6 : 7-dihydroxypteridine (45% yield).

7-*Hydroxypteridine and its derivatives.*

7-*Hydroxypteridine.*—4 : 5-Diaminopyrimidine (4·4 g., 0·04 mole), 5N-acetic acid (10 ml.), and sodium acetate trihydrate (10 g.) were dissolved in boiling water (40 ml.). Ethyl glyoxylate ethyl hemiacetal (9 g., 0·06 mole) was added and the mixture heated in a boiling water-bath, with occasional shaking, for 1 hour during which the pH fell from 6·5 to 5·5. The mixture was taken to pH 2·0 (metanil-yellow) with 5N-sulphuric acid (about 18 ml.), boiled for 5 minutes,

and chilled overnight. The crystals were filtered off and dissolved in boiling N-sodium hydroxide (70 ml.). The sodium salt of 7-hydroxypteridine crystallized in 2-cm. long, white needles which were collected after an hour at 20°, and dissolved in boiling water (70 ml.) containing N-sodium hydroxide (2 ml.). The boiling solution was brought to pH 2·5 (metanil-yellow) with 5N-sulphuric acid and chilled overnight. The *7-hydroxypteridine* was filtered off and recrystallized from 76 parts of boiling water. The yield was 65% of 0·5-cm. long, white plates, decomposing slowly at >230°. It is soluble in approx. 12 parts of boiling (and 70 parts at 20° dry pyridine, in 10 parts of boiling dimethylformamide (and in 6 parts of dimethylformamide azeotrope containing 6% of formic acid; in both cases 90% of the pteridine crystallizes on cooling), in 15 parts of boiling glacial acetic acid, and in 100 parts of boiling *n*-butanol. It is practically insoluble in acetone, ethanol, toluene, or light petroleum (Found: C, 48·6; H, 2·6; N, 37·4. $C_6H_4ON_4$ requires C, 48·65; H, 2·7; N, 37·8%.) Unlike 2-hydroxypteridine, it gave no colour with 10N-hydrochloric acid (1 day at 20°); it was destroyed on long boiling with N-sulphuric acid.

The above filtrate, at pH 2, was clarified with carbon and taken to pH 5·5 (bromocresol-green) with sodium citrate (4 g.) and 6N-sodium hydroxide, and refrigerated overnight. The crystals were recrystallized from the minimum of boiling water (about 390 ml.), giving 6-hydroxypteridine (see p. 1627) in 26% yield.

N-*Methyl-7-pteridone.*—A dried ethereal solution of diazomethane (0·026 mole in 20 ml.) was cooled to −70° and added portionwise, during 1 hour, to a stirred, ice-cold suspension of 7-hydroxypteridine (1·8 g., 0·012 mole) and its sodium salt (0·2 g.) in dry methanol (200 ml.). Stirring was continued for 2 hours and the reaction mixture left at 0° overnight. Undissolved solid (0·15 g.) was removed by filtration and the filtrate taken to dryness in a vacuum. The residue was extracted with boiling light petroleum (b. p. 60—80°; 100 + 50 ml.), leaving a large residue. The extracts were treated with charcoal and concentrated to 50 ml. On cooling of the solution, colourless crystals (0·8 g.; m. p. 114—119°) separated. These were dissolved in boiling light petroleum (b. p. 60—80°; 120 ml.) and this solution on cooling deposited 0·64 g. of presumed N-*methyl-7-pteridone* as white plates, m. p. 124·5—125·5° (32%) (Found: C, 52·0; H, 3·8; N, 35·1. $C_7H_6ON_4$ requires C, 51·85; H, 3·75; N, 34·55%). The combined mother-liquors, after concentration and cooling to 0°, deposited solid (0·29 g.; m. p. 93—103°). A sample (0·094 g.) of this material was heated under reflux with N-sodium hydroxide (2 ml.) for 5 minutes. On cooling of the solution, the sodium salt of 7-hydroxypteridine separated as white needles. These were collected and 0·014 g. of 7-hydroxypteridine was regenerated from them. This suggests that a trace of 7-methoxypteridine was formed, probably not more then 1% based on the 7-hydroxypteridine.

The Higher-melting Compound obtained from 7-Hydroxypteridine by Diazomethane.—(a) *Direct method.* A dried ethereal solution of diazomethane (25 ml., 0·03 mole) was added to a stirred ice-cooled suspension of 7-hydroxypteridine (1·5 g., 0·01 mole) in dry methanol (15 ml.). After 1 hour, evolution of nitrogen had ceased and a further portion of diazomethane (25 ml., 0·03 mole) was added. Stirring was continued for 2 hours and the pinkish-white crystalline product (0·95 g.; m. p. 144—145·5°) filtered off and washed with a little ice-cold methanol. A further crop (0·15 g.; m. p. 143—145°) was obtained by vacuum-concentration of the mother-liquor. Crystallization from methanol (15 parts) and treatment with charcoal gave white needles of presumed CN-*dimethyl-7-pteridone*, m. p. 146—147° (75% recovery) (Found: C, 54·30; H, 4·35; N, 31·9. $C_8H_8ON_4$ requires C, 54·55; H, 4·6; N, 31·8%).

(b) *By methylation of N-methyl-7-pteridone.* A dried ethereal solution of diazomethane (15 ml., 0·02 mole) was added in one portion to an ice-cooled suspension of *N*-methyl-7-pteridone (0·32 g., 0·002 mole) in dry methanol (5 ml.). Nitrogen was evolved and the reaction mixture was kept at 0° overnight. Ether and excess of diazomethane were then removed in a vacuum and the separated solid (0·27 g.; m. p. 141·5—143·5°) was collected by filtration. Sublimation at 130°/0·5 mm. gave white needles, m. p. 146—147°, not depressed on admixture with the compound described above.

Reduction of 7-Hydroxypteridine.—7-Hydroxypteridine (1·48 g., 0·01 mole) and sodium hydroxide (1·6 g., 0·04 mole) were dissolved in boiling water (120 ml.). Sodium dithionite dihydrate (4·2 g., 0·02 mole) was added during 3 minutes while the solution was vigorously boiled. The solution was rapidly concentrated to 60 ml. (pH 8), cooled in ice, and then brought to pH 4·8 with acetic acid (approx. 2·5 ml.), giving 1·6 g. (95%) of colourless crystals of *4-amino-5-carboxymethylaminopyrimidine* (IX), chromatographically homogeneous. For analysis, it was recrystallized from 19 parts of water (85% recovery). It decomposes about 310°, is very soluble in cold N-sodium hydroxide, and almost insoluble in all organic solvents (Found, for

material dried at 100°/0·1 mm.: C, 42·4; H, 4·6; N, 33·6. $C_6H_8O_2N_4$ requires C, 42·8; H, 4·8; N, 33·3%). The hydrochloride is sparingly soluble in cold N-hydrochloric acid.

4-Amino-5-carbomethoxymethylaminopyrimidine Dihydrochloride.—The above acid (0·34 g., 0·002 mole) was shaken for 4 hours with methanol (15 ml.) containing hydrogen chloride (2 g.). Air was blown through the solution until the volume fell to 2 ml. Anhydrous ether (5 ml.) was added and the chromatographically homogeneous, colourless crystals (0·37 g.) of the *ester dihydrochloride* were filtered off and dried in a vacuum at 20° (Found: C, 33·0; H, 4·55; Cl, 27·6. $C_7H_{10}O_2N_4,2HCl$ requires C, 33·0; H, 4·7; Cl, 27·8%). At pH 4·8, $\lambda_{max.}$ was 290 mμ; there was no absorption at 352 mμ (absence of 5 : 6-dihydro-7-hydroxypteridine). The R_F was 0·55 (dark spot); no spot characteristic of the free acid was seen, but a mixture of the acid and ester showed both spots in the correct positions.

5 : 6-Dihydro-7-hydroxypteridine was obtained in 70% yield by refluxing 4-amino-5-carboxymethylaminopyrimidine with 18 volumes (3 equiv.) of N-hydrochloric acid for 1 hour, and adjusting the pH of the hot solution to 5·5 with sodium citrate and sodium hydroxide. The chromatographically homogeneous, colourless crystals were recrystallized from 175 parts of boiling water (Found: C, 48·2; H, 3·9; N, 37·5. $C_6H_6ON_4$ requires C, 48·0; H, 4·0; N, 37·3%). The solubilities of this substance in organic solvents are very similar to those of 7-hydroxypteridine, but unlike the latter it is very soluble in cold 2N-sodium hydroxide and cold N-hydrochloric acid. Oxidation to 7-hydroxypteridine was carried out as in the case of 7 : 8-dihydro-6-hydroxypteridine (above); because 7-hydroxypteridine is much more soluble than the 6-isomeride, the mixed filtrates were evaporated to small bulk before being acidified.

Oxidation of 7-Hydroxypteridine to 6 : 7-Dihydroxypteridine.—7-Hydroxypteridine (1·2 g.) and yellow nitric acid (2·4 ml.; *d* 1·5) were mixed with cooling, and set aside at about 20° overnight. Water (24 ml.) was added. The pale yellow solution was boiled for 2 minutes and quickly cooled. Sodium citrate (1 g.) was dissolved in the solution, which was then brought to pH 4·5 with 6N-sodium hydroxide (about 8 ml.). The precipitate (0·6 g.) was purified through the potassium salt as described under 6 : 7-dihydroxypteridine (direct preparation) above. The yield was 30%.

We thank Dr. L. N. Short for the ultra-violet spectroscopy of 6- and 7-hydroxypteridine, and for the infra-red measurements, and also Mr. E. P. Serjeant for the remainder of the spectroscopy and for most of the potentiometry.

THE DEPARTMENT OF MEDICAL CHEMISTRY,
THE AUSTRALIAN NATIONAL UNIVERSITY,
183, EUSTON ROAD, LONDON, N.W.1.

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299. 1 : 9-*Pyrazoloanthrone.** *Part I. Replacement of Halogens in Derivatives of* 1 : 9-*Pyrazoloanthrone.*

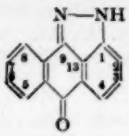
By WILLIAM BRADLEY and KENNETH W. GEDDES.

The 2- and 3-bromo- and 4-, 5-, and 8-chloro-derivatives of 1 : 9-pyrazoloanthrone * have been prepared and their behaviour towards aniline, piperidine, and sodium methoxide investigated. The relation between orientation and ease of replacement of a substituent is similar to that which obtains in the *meso*benzanthrone series. The two *N*-methyl derivatives of 1 : 9-pyrazoloanthrone have been prepared and several of their halogeno-drivatives. The properties of the halogen compounds are generally similar to those of the parent 1 : 9-pyrazoloanthrone.

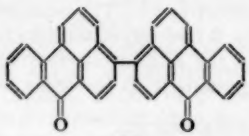
1 : 9-PYRAZOLOANTHRONE * (I) resembles *meso*benzanthrone in its ability to undergo self-condensation. When heated with alcoholic potassium hydroxide, *meso*benzanthrone affords di*meso*benzanthron-4-yl (II) (Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 259), and in similar circumstances 1 : 9-pyrazoloanthrone yields di-(1 : 9-pyrazoloanthron-2-yl) (III) (Mayer and Heil, *Chem.-Ztg., Fortschrittsber.*, 1929, p. 56).

* The systematic name for a substance of structure (I) would be pyrazolo(5′ : 4′ : 3′-1 : 13 : 9)anthrone, and that for the isomer with hydrogen attached to the other nitrogen atom would be pyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone. Although formula (I) is used in this paper the position of the hydrogen atom cannot be allocated, and the less determinate name, 1 : 9-pyrazoloanthrone is therefore used. ED.

With *meso*benzanthrone the capacity for self-condensation is related to its ability to undergo direct substitution by bases, including the anions of weak acids, and to the ease with which halogen substituents are replaced at positions 4 and 6 (Bradley, *J.*, 1937, 1091; 1948, 1175; Bradley and Jadhav, *J.*, 1937, 1791; 1948, 1622, 1748). For the latter reason it was of interest to study the replacement of halogen substituents in derivatives of 1 : 9-pyrazoloanthrone.



(I)



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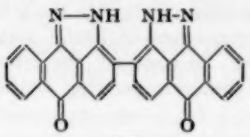
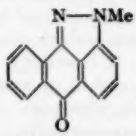


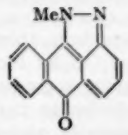
(III)

Of the several routes to 1 : 9-pyrazoloanthrone (cf. B.I.O.S. Report No. 987, p. 128; B.P. 297 366) we found Mohlau's method (*Ber.*, 1912, **45**, 2244) to be the most satisfactory. Mohlau described the preparation of 8-chloro-1 : 9-pyrazoloanthrone, and we have used the same procedure in preparing the 2- and 3-bromo- and 4- and 5-chloro-derivatives.

An 8-chloro-substituent proved inert towards various bases, one in position 5 was replaced by piperidine, but not by sodium methoxide or aniline; a 4-chloro-substituent was replaced by each of the three reagents, and by hydrazine. The halogen substituent of 2-bromo-1 : 9-pyrazoloanthrone was replaced by piperidine and sodium methoxide, but that of the 3-bromo-isomer was inert. The results harmonise with those obtained earlier with *meso*benzanthrone in which it was found that halogen substituents situated *ortho* or *para* to the carbonyl group may be replaced. In addition the effect of the carbonyl group is transmitted more easily through the indazole nucleus of 1 : 9-pyrazoloanthrone than through the other benzene nucleus.

Attention has also been given to the two *N*-methyl-1 : 9-pyrazoloanthrones (IV and V), because they should exhibit different degrees of nuclear reactivity. The formation of a methyl derivative, m. p. 221—224°, by methyl alcohol and sulphuric acid was recorded in G.P. 454 760. Later G.P. 456 763 and 479 284 mentioned the formation of two methyl derivatives when sodium hydroxide and methyl sulphate were used. A methyl derivative, m. p. 189°, was prepared by the action of methylhydrazine on 1-chloroanthraquinone (B.P. 470 475). We have confirmed the formation of the compound, m. p. 189°, and regard it as 1'-methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone (IV) because Blanksma and Wackers (*Rec. Trav. chim.*, 1936, **55**, 655) found that methylhydrazine reacts at the secondary amine group with picryl chloride and 1-chloro-2 : 4-dinitrobenzene.

(IV)




(V)

Repeating the methylation of 1 : 9-pyrazoloanthrone with sodium hydroxide and methyl sulphate and separating the alkali-insoluble products by chromatography we obtained two derivatives, (*a*) m. p. 189°, identical with that mentioned above, and (*b*) m. p. 229°, which appeared to be a purer form of the product, m. p. 221—224°. The constitution (IV) having been assigned, the isomer, m. p. 229°, must be 1'-methylpyrazolo-(3' : 4' : 5'-1 : 13 : 9)anthrone (V). Maki and Akamastsu (Ann. Meeting Soc. Chem. Ind. Japan, 1949; Rep. Jap. Assoc. Promotion Sci., 1949) reported *N*-methyl derivatives, m. p. 189° and 154·5°, respectively. Whilst the former is the compound (IV) we have obtained some of the isomer, m. p. 229°, from the product of m. p. 154·5°.

Using Mohlau's method (*loc cit.*), but methylhydrazine instead of hydrazine, we have prepared 2-methyl- and 3-bromo-derivatives of (IV). An attempt to prepare (IV) by reducing the *N*-nitroso-derivative of 1-methylaminoanthraquinone (G.P. 442 312) was unsuccessful.

Bromination of (V) gave the 2-bromo-derivative identical with one of the products

obtained by methylating 2-bromo-1 : 9-pyrazoloanthrone with alkali and methyl sulphate. Bromination of (IV) occurred at position 4.

4-Bromo-1'-methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone heated with methanolic sodium methoxide afforded the corresponding 4-hydroxy-derivative, also obtained by the action of alkali hydroxides on 4-chloro-1'-methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone which was prepared from 1 : 4-dichloroanthraquinone by methylhydrazine. In its reaction with sodium methoxide the 4-bromo-derivative of (IV) resembles the similarly constituted 6-chloro*meso*benzanthrone which yields 6-hydroxy*meso*benzanthrone in similar circumstances. In contrast, the 2-bromo- and the 4-chloro-derivative of 1 : 9-pyrazoloanthrone afford the corresponding methoxy-compounds with the same reagent.

Experimental

1 : 9-Pyrazoloanthrone was prepared from 1-chloroanthraquinone by the hydrazine method (Mohlau, *loc. cit.*).

1 : 2-*Dibromoanthraquinone*.—1-Amino-2-bromoanthraquinone (50 g.) (Grandmougin, *Compt. rend.*, 1921, **173**, 839) was stirred at room temperature during 4 hours with a solution prepared from sodium nitrite (18 g.) and concentrated sulphuric acid (150 c.c.). The product was added to ice, and the precipitated diazonium salt collected and added to a suspension of cuprous bromide in 50% (w/w) hydrobromic acid (200 c.c.). [The cuprous bromide was prepared from copper sulphate (180 g.), sodium bromide (120 g.), and sodium sulphite (50 g.).] Nitrogen was liberated, and the suspension was warmed for a few minutes to complete the reaction and then mixed with water. The precipitate was collected, stirred with warm dilute nitric acid, then separated, washed, and dried. Recrystallisation from chlorobenzene gave pale yellow needles (39·5 g.), m. p. 223° (Battegay, *Bull. Soc. chim.*, 1921, [iv], **29**, 1017, records m. p. 223°).

2-*Bromo*-1 : 9-*pyrazoloanthrone*.—Hydrazine hydrate (4·25 g. of a 50% solution) was added to a solution containing 1 : 2-dibromoanthraquinone (8·5 g.) in pyridine (150 c.c.). Heating under reflux caused a deep red colour to develop, changing to yellow after 5 hours. The product was added to water, and the precipitate was collected, washed, dried (7 g.; m. p. 265—272°), and then recrystallised from nitrobenzene. The resulting brown solid, m. p. 285—287°, was further purified by vacuum-sublimation or by chromatography on alumina and obtained as yellow needles, m. p. 289—290° (Found: C, 56·4; H, 2·35; N, 9·7; Br, 27·5. $C_{14}H_7ON_2Br$ requires C, 56·2; H, 2·5; N, 9·4; Br, 26·7%). 2-*Bromo*-1 : 9-*pyrazoloanthrone* forms an orange solution in aqueous sodium hydroxide, changed to greenish-yellow on addition of sodium dithionite. The pale greenish-yellow solution in pyridine becomes pink on addition of a drop of concentrated methyl alcoholic potassium hydroxide (Bradley and Leete, *J.*, 1951, 2132). The compound forms an orange solution in concentrated sulphuric acid. The *N*-acetyl derivative had m. p. 205° (from chlorobenzene); G.P. 457 182 records m. p. 209—211°.

3-*Bromo*-1 : 9-*pyrazoloanthrone*.—Prepared from 1 : 3-dibromoanthraquinone (12 g.) and hydrazine hydrate (6 g. of a 50% aqueous solution) this *compound* had m. p. 273—279° (yield, 10 g.). Recrystallisation from chlorobenzene gave yellow, minute needles, m. p. 309—310° (Found: N, 9·1. $C_{14}H_7ON_2Br$ requires N, 9·4%). It dissolves with an orange colour in aqueous sodium hydroxide; a greenish-yellow solution results on addition of sodium dithionite. The greenish-yellow solution in pyridine becomes yellowish-pink on the addition of methyl alcoholic potassium hydroxide, and a yellow fluorescence develops.

The *N*-acetyl derivative crystallised when 3-bromo-1 : 9-pyrazoloanthrone (10 g.) was heated under reflux for 10 minutes with acetic anhydride (10 c.c.). The pale yellow needles were collected, washed with alcohol, and dried, and had m. p. 222—224° (8·5 g.). Recrystallisation from chlorobenzene gave pale yellow, minute needles, m. p. 228°.

4-*Chloro*-1 : 9-*pyrazoloanthrone*.—Prepared according to B.P. 345 748 from hydrazine hydrate and 1 : 4-dichloroanthraquinone (Ullmann, *Ber.*, 1920, **53**, 826). The product crystallised from chlorobenzene had m. p. 318° (Found: C, 65·7; H, 3·0; N, 10·7; Cl, 14·15. Calc. for $C_{14}H_7ON_2Cl$: C, 65·9; H, 2·8; N, 11·0; Cl, 14·0%). B.P. 345 748 records m. p. 301—302°. The orange solution in aqueous sodium hydroxide becomes yellow on the addition of sodium dithionite. The pale yellow solution in pyridine changes to orange and develops a green fluorescence on the addition of methyl alcoholic potassium hydroxide. It forms an orange solution in concentrated sulphuric acid.

5-*Chloro*-1 : 9-*pyrazolocnthrone*.—1 : 5-Dichloroanthraquinone (20 g.), hydrazine hydrate (5 g.), and pyridine (175 c.c.) were heated under reflux for 5 hours, and then the product (m. p. 240—245°; 18·8 g.) was isolated. It was dissolved in concentrated sulphuric acid, heated to

100°, and then recovered (m. p. 275—285°) by addition of the mixture to water. Recrystallisation from chlorobenzene gave golden-yellow flakes, m. p. 298° (Found : C, 65·5; H, 3·0; N, 11·0; Cl, 14·4. $C_{14}H_7ON_2Cl$ requires C, 65·9; H, 2·8; N, 11·0; Cl, 14·0%). It resembled the isomeric 4-chloro-derivative in its colour reactions with sodium hydroxide, alkaline sodium dithionite, pyridine and methyl alcoholic potassium hydroxide, and concentrated sulphuric acid.

The compound (8 g.) was heated for 20 minutes with acetic anhydride (50 c.c.). On cooling, the *acetyl* derivative crystallised in brown needles, m. p. 249° (Found : N, 9·9; Cl, 11·6. $C_{16}H_9O_2N_2Cl$ requires N, 9·4; Cl, 11·9%).

8-*Chloro*-1 : 9-*pyrazoloanthrone.*—Prepared by Mohlau's method (*loc. cit.*), the product crystallised from xylene in yellow needles, m. p. 346—347° (Found : N, 11·0. Calc. for $C_{14}H_7ON_2Cl$: N, 11·0%). Mohlau records m. p. >360°.

The *acetyl* derivative (7 g.) separated when 8-chloro-1 : 9-pyrazoloanthrone (8 g.) was refluxed for 10 minutes with acetic anhydride (60 c.c.). Recrystallisation from chlorobenzene gave pale yellow needles, m. p. 280° (Found : C, 64·3; H, 3·0; N, 9·5; Cl, 12·3. $C_{16}H_9O_2N_2Cl$ requires C, 64·5; H, 3·1; N, 9·4; Cl, 11·9%).

Methylation of 1 : 9-*Pyrazoloanthrone.*—(*a*) 1 : 9-Pyrazoloanthrone (11 g.) was treated with methyl sulphate (25 g.), sodium hydroxide (10·5 g.), water (100 c.c.), and alcohol (50 g.) according to G.P. 479 284. The product (10·1 g.; m. p. 152—162°) could not be purified satisfactorily by crystallisation from alcohol or chlorobenzene. The product (10 g.) was chromatographed in benzene on alumina. A broad yellow band formed was eluted by 100-c.c. portions of benzene. The several extracts were collected and evaporated, yielding : (i) 1'-Methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone, yellow needles, m. p. 189° (Found : C, 76·7; H, 4·4; N, 11·6. Calc. for $C_{15}H_{10}ON_2$: C, 76·9; H, 4·3; N, 12·0%) (5·4 g.). These dissolved in benzene forming a yellow solution having a vivid blue fluorescence. They were insoluble in aqueous sodium hydroxide ; on addition of sodium dithionite a pale yellow solution was formed. The yellow solution in pyridine remained unaltered on addition of solid potassium hydroxide. The same reagent added to a solution in acetone caused a slow change to dull red. (ii) 1'-Methylpyrazolo(3' : 4' : 5'-1 : 13 : 9)anthrone, yellow needles, m. p. 229° (Found : C, 76·6; H, 4·1; N, 12·1%), which afforded a yellow solution with a bright yellowish-green fluorescence in benzene. The behaviour with sodium hydroxide, sodium dithionite, and pyridine–potassium hydroxide was identical with that of the isomer. Its yellow solution in acetone, however, changed rapidly through red and violet to blue on the addition of alkali. (iii) A mixture, m. p. 150—160° (1·6 g.), from the middle of the column.

(*b*) 1 : 9-Pyrazoloanthrone (20 g.) was treated with methyl alcohol (30 g.) and concentrated sulphuric acid (120 g.) as described in G.P. 454 760. The product (13 g.) crystallised from chlorobenzene as yellow needles, m. p. 224° (Found : C, 76·5; H, 4·1; N, 12·4%), identical in its reactions with the isomer (ii), m. p. 229°.

(*c*) 1-Chloroanthraquinone (7·5 g.) was treated for 12 hours with methylhydrazine sulphate (5 g.) in pyridine (75 c.c.) containing anhydrous potassium carbonate (7 g.), according to the procedure of B.P. 470 475. The product (7 g.), m. p. 151—156°, crystallised from chlorobenzene as yellow needles (5 g.), m. p. 187—189° (Found : C, 76·9; H, 4·6; N, 11·6%), which did not depress the m. p. of the isomer (i).

In a second preparation, the constituents of the pyridine mother-liquor obtained at the first stage were examined. Addition of water gave a yellow solid (3·5 g.) which crystallised from alcohol (m. p. 141—143°). Chromatography from benzene on alumina afforded material, m. p. 151—152° (Found : N, 6·2; Cl, 7·8%), which gave the reactions of an anthraquinone derivative and melted at 160—170° when mixed with the isomer, m. p. 189°.

1-N-*Methyl*-N-*nitrosoaminoanthraquinone.*—1-Methylaminoanthraquinone afforded the N-*nitroso*-derivative with sodium nitrite and acetic acid (G.P. 422 312). This crystallised from chlorobenzene as golden yellow needles, m. p. 185—186° (Found : C, 67·8; H, 3·6; N, 10·4. $C_{15}H_{10}O_3N_2$ requires C, 67·7; H, 3·8; N, 10·5%), and gave a positive Liebermann reaction. When heated with alcohol (150 c.c.) and sodium sulphide (2 g.) for 1·5 hours it (2 g.) gave 1-methylaminoanthraquinone, m. p. 169—170°, not depressed by admixture with the authentic compound. The same compound resulted when the nitrosamine (1·5 g.) was heated under reflux for 6 hours with pyridine (40 c.c.) containing hydrazine hydrate (0·7 g.). Finally, the nitrosamine (3 g.), stirred with zinc dust (10 g.) and a mixture of acetic acid (100 g.) and water (100 g.) at 20°, yielded a product, m. p. 150—152°, consisting mainly of 1-methylaminoanthraquinone.

2-*Bromo*-1'-*methylpyrazolo*(5' : 4' : 3'-1 : 13 : 9)*anthrone.*—1 : 2-Dibromoanthraquinone (4 g.), methylhydrazine sulphate (2·5 g.), pyridine (40 c.c.), and sodium acetate (3 g.) were refluxed for

10 hours. Next morning the precipitate was collected, washed with water, and dried (1 g.; m. p. 206—207°). Vacuum-sublimation gave a yellow *compound*, m. p. 224—227° (Found: N, 9·1; Br, 25·2. $C_{15}H_9ON_2Br$ requires N, 8·9; Br, 25·6%), not depressed on admixture with the compound, m. p. 230°, obtained as fraction (i) in the methylation of 2-bromo-1 : 9-pyrazoloanthrone (see below).

2-*Bromo*-1′-*methylpyrazolo*(3′ : 4′ : 5′-1 : 13 : 9)*anthrone*.—A solution of bromine (1·5 g.) in acetic acid (10 c.c.) was added slowly, with stirring, to one of 1′-methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone (2 g.) in acetic acid (20 c.c.). After 2 hours at the room temperature a yellow solid had separated, and this was collected, washed free from acid, and dried (2·1 g., m. p. 198—226°). Recrystallisation from chlorobenzene gave the *bromo*-compound as yellow crystals, m. p. 232—234° (Found: N, 8·9; Br, 26·0%).

Methylation of 2-*Bromo*-1 : 9-*pyrazoloanthrone*.—Methyl sulphate (17 g.) was stirred for 3 hours at the room temperature with a solution of 2-bromo-1 : 9-pyrazoloanthrone (10 g.) and sodium hydroxide (7 g.) in water (70 c.c.). The product which separated was collected, digested with a solution of sodium hydroxide in aqueous ethyl alcohol, then washed, and dried (9 g.; m. p. 185—190°), and a portion (5 g.) was chromatographed from benzene on alumina. A broad yellow band formed, becoming brownish-yellow at the top of the column. Benzene was passed through the column, and each successive 200 c.c. of eluate was concentrated to crystallisation. The following fractions resulted, in order: (i), m. p. 230° (0·6 g.); (ii), m. p. 226—229° (1·2 g.); (iii), m. p. 180—190° (1·9 g.); (iv), m. p. 170—185° (0·2 g.); (v), m. p. 180—216° (0·2 g.); (vi), m. p. 226—232° (0·1 g.). Fraction (vi) (Found: N, 8·9%) did not depress the m. p. of the preceding product, m. p. 232—234°. Fraction (i) (Found: C, 57·3; H, 3·2; N, 8·9; Br, 25·4%) was identical with the product obtained from 1 : 2-dibromoanthraquinone (see above).

3-*Bromo*-1′-*methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone*.—1 : 3-Dibromoanthraquinone (10 g.), methylhydrazine sulphate (5 g.), pyridine (125 c.c.), and potassium carbonate (7 g.) were refluxed for 12 hours and then kept overnight. The precipitated greenish-yellow needles of the *pyrazoloanthrone* were collected, washed, and dried (4 g.; m. p. 242—244°) (Found: C, 57·5; H, 3·1; N, 8·8; Br, 25·6%).

4-*Chloro*-1′-*methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone*.—Prepared analogously from 1 : 4-dichloroanthraquinone (5 g.), methylhydrazine sulphate (5 g.), sodium carbonate (7 g.), and pyridine (50 c.c.) by 8 hours' refluxing, the *chloro*-compound (2 g.) had m. p. 260° (Found: C, 67·1; H, 3·7; N, 10·8. $C_{15}H_9ON_2Cl$ requires C, 67·1; H, 3·4; N, 10·5%) after sublimation *in vacuo*.

2 : 1′-*Dimethylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone*.—Prepared similarly from 1-chloro-2-methylanthraquinone, the *methyl* analogue crystallised from chlorobenzene as yellow needles, m. p. 217—218° (Found: N, 10·8. $C_{16}H_{12}ON_2$ requires N, 11·2%).

4-*Bromo*-1′-*methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone*.—Bromine (2·5 g.) in acetic acid (10 c.c.) was added to a warm solution of 1′-methylpyrazolo(5′ : 4′ : 3′-1 : 13 : 9)anthrone (3 g.) in acetic acid (50 c.c.). After an hour's refluxing the product was added to water, and the yellow precipitate was collected, washed, and dried (2·6 g.; m. p. 170—180°). Repeated crystallisation from chlorobenzene gave this *compound* as yellow, minute needles, m. p. 248—249° (Found: C, 57·8; H, 2·9; N, 9·2; Br, 25·7%).

Replacement Reactions.—4-*Anilino*-1 : 9-*pyrazoloanthrone*. 4-Chloro-1 : 9-pyrazoloanthrone (0·5 g.) and freshly distilled aniline (5 g.) were heated under reflux for 3 hours. On cooling, a pale brown solid separated. It was collected, washed with dilute hydrochloric acid, then water, and finally dried. The product (0·35 g.; m. p. 260—270°) was chromatographed on alumina from benzene. The main band was orange; it was accompanied by pink and blue bands. The orange region was extruded and the adsorbed material extracted with acetone. Evaporation afforded material, m. p. 272—273°, and this crystallised from chlorobenzene in golden-orange needles, m. p. 282—283° (Found: N, 13·4. $C_{20}H_{13}ON_3$ requires N, 13·5%). The *anilino*-compound dissolved in concentrated sulphuric acid to an orange solution. In pyridine it was pale yellow, and orange on the addition of methyl alcoholic potassium hydroxide.

4-*Piperidino*-1 : 9-*pyrazoloanthrone*, prepared similarly by heating 4-chloro-1 : 9-pyrazoloanthrone (0·2 g.) with piperidine (2 g.), crystallised from chlorobenzene as yellow needles, m. p. 264° (Found: N, 13·7. $C_{19}H_{17}ON_3$ requires N, 13·8%). The solution in concentrated sulphuric acid was pale yellow. It formed a bright yellow solution in 20% sodium hydroxide solution, showing a greenish yellow fluorescence; the fluorescence disappeared on addition of sodium dithionite. The yellow solution in pyridine became orange and developed a greenish-yellow fluorescence on addition of potassium hydroxide.

4-*Methoxy*-1 : 9-*pyrazoloanthrone*. 4-Chloro-1 : 9-pyrazoloanthrone (0·5 g.) was heated under reflux for 3 hours with a solution prepared from sodium (2·5 g.) and methanol (25 c.c.).

After cooling, and addition of dilute hydrochloric acid, a pale yellow solid separated. This *methoxy*-derivative was collected, washed, and dried (0·35 g.; m. p. 270—274°), and was obtained by crystallisation from chlorobenzene as a pale yellow solid, m. p. 287—288° (Found: N, 11·0; OMe, 9·8. $C_{15}H_{10}O_2N_2$ requires N, 11·2; OMe, 12·4%). It dissolved in 20% aqueous sodium hydroxide with a yellow colour and a green fluorescence.

4-*Hydrazino*-1 : 9-*pyrazoloanthrone.* Hydrazine hydrate (0·75 g.), pyridine (25 c.c.), and 4-chloro-1 : 9-pyrazoloanthrone were heated at 140° for 10 hours. Brown needles separated, and these were collected, washed, dried (1 g.), and sublimed *in vacuo*. The *product* had m. p. 270° (Found: N, 21·8. $C_{14}H_{10}ON_4$ requires N, 22·4%). It was sparingly soluble in hot water, forming a pale yellow solution with a green fluorescence. It gave a similar solution in pyridine; on addition of methyl alcoholic potassium hydroxide a yellow solution resulted with a bright-orange fluorescence. It was recovered unaltered after being stirred in concentrated sulphuric acid at 90° for 15 minutes.

5-*Piperidino*-1 : 9-*pyrazoloanthrone.* 5-Chloro-1 : 9-pyrazoloanthrone (0·5 g.) and piperidine (5 g.) were heated under reflux for 3 hours. The reddish-orange solution was cooled and added to water, and the orange precipitate collected, washed, and dried (0·4 g.; m. p. 205—210°). Recrystallisation from chlorobenzene gave the *piperidino*-compound as yellow needles, m. p. 218—219° (Found: N, 13·5. $C_{19}H_{17}ON_3$ requires N, 13·8%). It dissolved in concentrated sulphuric acid with a bright yellow, and in sodium hydroxide with a wine-red colour, the latter becoming yellow on the addition of sodium dithionite. The yellow solution in pyridine became pinkish-yellow on addition of methyl alcoholic potassium hydroxide.

5-Chloro-1 : 9-pyrazoloanthrone (0·5 g.) was recovered unaltered after 4 hours' refluxing with a solution of sodium (2·5 g.) in methanol (25 c.c.). Heated with aniline (5 g.) for 3 hours under reflux, 5-chloro-1 : 9-pyrazoloanthrone (0·5 g.) afforded mainly unchanged material (m. p. 220—240° (Found: N, 11·1; Cl, 6·7%).

8-Chloro-1 : 9-pyrazoloanthrone did not react with piperidine at the b. p. during 21 hours, or with aniline at the b. p. during 3 hours.

2-*Piperidino*-1 : 9-*pyrazoloanthrone.* 2-Bromo-1 : 9-pyrazoloanthrone (0·5 g.) heated under reflux for 3 hours with piperidine (5 g.) afforded a product, m. p. 216—250° (0·4 g.), which, after crystallisation from chlorobenzene, had m. p. 251—252° (Found: N, 13·4. $C_{19}H_{17}ON_3$ requires N, 13·8%). This *derivative* dissolved in concentrated sulphuric acid with a pale yellow colour, and in sodium hydroxide with an orange colour becoming yellow on the addition of sodium dithionite. The yellow solution in pyridine exhibited a pale green fluorescence; on addition of methanolic potassium hydroxide the yellow colour deepened and a yellow fluorescence developed.

2-*Methoxy*-1 : 9-*pyrazoloanthrone.* 2-Bromo-1 : 9-pyrazoloanthrone (0·5 g.), heated for 3 hours with a solution of sodium (2·5 g.) in methanol (25 c.c.), afforded 0·4 g. of the *methoxy*-compound, yellow needles, m. p. 224—226° (from chlorobenzene) (Found: N, 10·9; OMe, 10·4. $C_{15}H_{10}O_2N_2$ requires N, 11·2; OMe, 12·4%). It dissolved in aqueous sodium hydroxide with a yellow colour and a green fluorescence.

Action of Reagents on 3-*Bromo*-1 : 9-*pyrazoloanthrone.*—3-Bromo-1 : 9-pyrazoloanthrone was recovered after being heated under an excess of sodium methoxide (4 hours), aniline (3 hours), or piperidine (6 hours). It was also recovered mainly unchanged after 12 hours in boiling ethanolic potassium hydroxide (3·5 g. in 7 c.c.): a product, m. p. 280—285°, was obtained by vacuum-sublimation of the crude product.

4-*Hydroxy*-1′-*methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone.*—(*a*) 4-Bromo-1′-methylpyrazolo-(5′ : 4′ : 3′-1 : 13 : 9)anthrone (0·4 g.) was heated under reflux with a solution of sodium (4 g.) and methanol (40 c.c.). After addition of water and dilute hydrochloric acid the methanol was distilled off, and the yellow precipitate was collected, washed, and dried (0·3 g.) It was extracted with aqueous sodium hydroxide, and the solution was filtered and then acidified, giving the 4-*hydroxy*-derivative, m. p. 204—205° (Found: N, 11·4. $C_{15}H_{10}O_2N_2$ requires N, 11·2%).

(*b*) The same derivative, m. p. 206—208°, resulted when 4-chloro-1′-methylpyrazolo-(5′ : 4′ : 3′-1 : 13 : 9)anthrone was heated with methanolic sodium methoxide under the same conditions.

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CLOTHWORKERS RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

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300. 1 : 9-*Pyrazoloanthrone. Part II.* Nuclear Substitution by Bases and Self-condensation in* 1 : 9-*Pyrazoloanthrone and its* N-*Methyl Derivatives.*

By William Bradley and Kenneth W. Geddes.

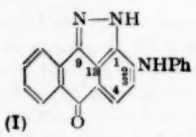
1 : 9-Pyrazoloanthrone and its *N*-methyl derivatives readily undergo nuclear substitution by reactive anions, for example, that of sodium anilide. The substituting anion enters the indazole nucleus and replaces hydrogen in the *para*-position to the carbonyl group. 1'-Methylpyrazolo(3' : 4' : 5'-1 : 13 : 9)anthrone is more easily substituted than the isomeric 1'-methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone. The difference is attributed to bond-fixation, which results in a higher degree of unsaturation in the case of the first isomer.

1 : 9-Pyrazoloanthrone and its *N*-methyl derivatives undergo self-condensation in the presence of bases. The constitutions of the products have been determined, and the results have been applied to decide the structures of the products which are obtained by methylating di-(1 : 9-pyrazolo-2-anthronyl). The structural factors which affect the self-condensation have been investigated, and the steps in the condensation process are discussed.

1 : 9-Pyrazoloanthrone and its *N*-methyl derivatives, as well as di-(1 : 9-pyrazolo-2-anthronyl), are hydrolysed by fused alkalis. The constitutions of the resulting acids are considered.

In Part I * it was shown that 1 : 9-pyrazoloanthrone resembles *meso*benzanthrone in the properties of its halogen derivatives. The present communication describes experiments on the direct replacement of nuclear hydrogen in 1 : 9-pyrazoloanthrone by bases, including anions, and the self-union of 1 : 9-pyrazoloanthrone and its *N*-methyl derivatives.

1 : 9-Pyrazoloanthrone reacts with sodium anilide to form 2-anilino-1 : 9-pyrazoleanthrone (I), identical with the compound formed by the action of sodium anilide on 2-bromo-1 : 9-pyrazoloanthrone. A similar compound is formed when the sodium derivative of *o*-toluidine is used. In these reactions 1 : 9-pyrazoloanthrone resembles *meso*benzanthrone (Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 258). When heated with potassium hydroxide and an oxidant, *meso*benzanthrone affords a mixture of 4- and 6-hydroxy*meso*benzanthrone (Bradley and Jadhav, *J.*, 1937, 1791). 1 : 9-Pyrazoloanthrone does not behave in this way; the main product is an acid, either (II) or (III). It is probably (II) since ring-opening is dependent on the presence of the indazole nucleus. Heating with sulphuric acid re-forms 1 : 9-pyrazoloanthrone. Alkaline oxidation of 1 : 9-pyrazoloanthrone yields also a small quantity of a phenolic substance, possibly a hydroxy-derivative of (II).



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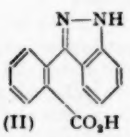

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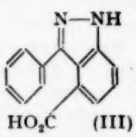
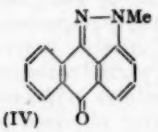


(III)

The *N*-methyl derivative (IV), m. p. 189°, of 1 : 9-pyrazoloanthrone reacted analogously with sodium anilide to form the 2-anilino-derivative (V). Alkaline oxidation of (IV) yielded an acid whence (IV) was regenerated by hot sulphuric acid. The acid was probably (VI) for a reason similar to that already mentioned. It was accompanied by a phenolic product, possibly a hydroxy-derivative of (VI). The *N*-methyl-1 : 9-pyrazoloanthrone (IV), gave a yellow solution in acetone which slowly became dull red after solid potassium hydroxide had been added, resembling *meso*benzanthrone which affords a deep green solution in similar circumstances (B.P. 319,593; 322,253).

* Part I, preceding paper.

The *N*-methyl derivative, m. p. 229° (VII), was much more reactive towards amines, alkalis in the presence of oxidants, and acetone containing an alkali hydroxide. With sodium anilide substitution was not observed but, instead, mainly coupling of two molecules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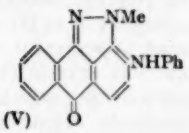
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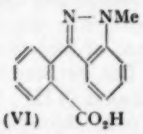
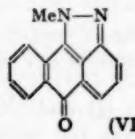

(VI)

occurred, to form (VIII). An acetone solution of (VII), to which solid potassium hydroxide was added, rapidly became red, and then, through violet, blue. The blue colour was probably that of (IX). The reaction occurred much more readily than with (IV).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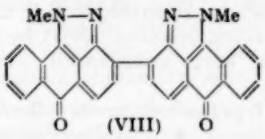
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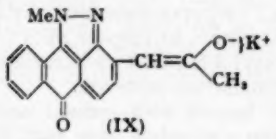
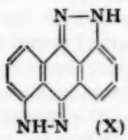

(IX)

1 : 9-5 : 10-Dipyrazoloanthracene * (X) (Mohlau, *Ber.*, 1912, **45**, 2244) does not react with sodium anilide, and is recovered unaltered after fusion with potassium hydroxide and manganese dioxide.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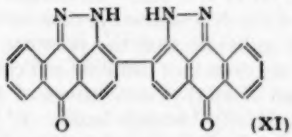
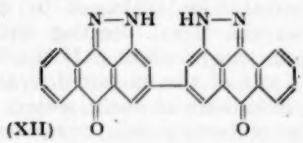
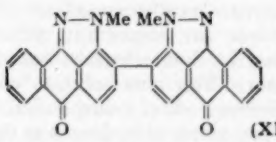

(XI)

The properties of (X) show clearly how essential is the carbonyl group for the reactivity of pyrazoloanthrone and its *N*-methyl derivatives towards bases. The derivative (VII) is much more reactive than (V), probably because in (VII) the nucleus carrying the carbon atoms 2, 3, and 4 approaches more closely a typical open-chain aliphatic αβ-unsaturated ketone in the degree of its unsaturation.

Conversion of 1 : 9-pyrazoloanthrone into a yellow colouring matter by hot alcoholic potassium hydroxide was first described in G.P. 255,641. Conversion of the product into a potassium salt and alkyl derivatives followed G.P. 301,554, 302,259, 302,260). Mayer and Heil first (*Ber.*, 1922, **55**, *B*, 2155) proposed a highly condensed structure but later (*Chem.-Ztg., Fortschrittber.*, 1929, **56**) showed that the product of the alkali fusion was di-(1 : 9-pyrazoloanthron-2-yl) (XI).


(XII)


(XIII)

A more detailed study of the alkylation of (XI) (G.P. 301,554, 302,259, 302,260) has shown that mono- and di-alkyl derivatives can be prepared, and that the dialkyl compounds exist in two forms (G.P. 359,139, 463,246): methylation is stated to yield an orange dimethyl derivative, m. p. 350°, soluble in chlorobenzene, and an insoluble red dimethyl derivative. The latter derivative differs also in separating from sulphuric acid as a sulphate. The red derivative results directly by the alkali fusion of one, and only one, of the *N*-methyl derivatives of 1 : 9-pyrazoloanthrone (G.P. 456,763, 479,284). Maki and Akamastsu (Ann. Meeting Soc. Chem. Ind. Japan, 1949; Rept. Jap. Assoc. Promotion

* For numbering see footnote, p. 1630.

Sci., 1949) prepared two monoethyl derivatives of 1 : 9-pyrazoloanthrone; one isomer, of m. p. 145°, yields a red colouring matter when it is fused with alkali, whilst the other, of m. p. 186·5°, remains unchanged. Maki and Akamastsu consider that steric factors determine the result and regard the *N*-ethyl compound, m. p. 145°, and the derived red colouring matter as the ethyl analogues of (VII) and (VIII) respectively. Structure (IV; Et in place of Me) then remains to represent the *N*-ethyl-1 : 9-pyrazoloanthrone, m. p. 186·4°. The authors also point out that in (VII) " partial valency exists in the 2-position," and that (VIII; Et in place of Me), which is insoluble in chlorobenzene, must represent the red, chlorobenzene-insoluble colouring matter obtained by the direct ethylation of (XI).

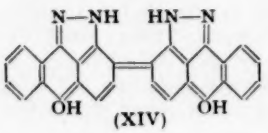
In the present experiments it was found that *N*-acetyl-2-bromo-1 : 9-pyrazoloanthrone gave (XI) directly when it was heated with copper in naphthalene, deacetylation having occurred in the reaction. The product was identical with the colouring matter obtained from 1 : 9-pyrazoloanthrone by alkali fusion as described in G.P. 255,641.

Attempts to prepare di-(1 : 9-pyrazoloanthron-3-yl) (XII) by the action of copper on *N*-acetyl-3-bromo-1 : 9-pyrazoloanthrone were unsuccessful; both deacetylation and debromination occurred.

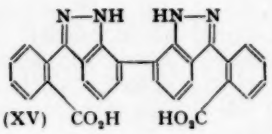
If heated with sodium anilide 1 : 9-pyrazoloanthrone afforded both (I) and (XI). Sodium *o*-toluidide gave both 2-*o*-toluidino-1 : 9-pyrazoloanthrone and (XI), but neither self-coupling nor nuclear substitution occurred when the condensing agent was sodium diphenylamide.

Sodium anilide and (IV) gave 2-anilino-1'-methylpyrazolo(5' : 4' : 3'-1 : 13 : 9)anthrone (V) and (XIII); the latter is a yellowish-orange colouring matter, m. p. 357°, identical in reactions with one of the *NN'*-dimethyl derivatives prepared by the methylation of (XI). Formation of (XIII) indicates that the presence of a methyl group near the 2-position of 1 : 9-pyrazoloanthrone does not inhibit self-condensation, and that the difference in behaviour of the two *N*-methyl derivatives of 1 : 9-pyrazoloanthrone is the result of a difference in their reactivity towards bases. If (XIII) is the constitution of the orange-yellow dimethyl derivative of pyrazoloanthrone-yellow (XI), the red derivative formed simultaneously during methylation with methyl sulphate and alkali is probably (VIII).

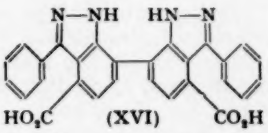
1 : 9-5 : 6-Dipyrazoloanthracene (X) was recovered unaltered after being heated with sodium anilide, ethyl alcoholic potassium hydroxide, or a mixture of manganese dioxide and potassium hydroxide.



(XIV)



(XV)



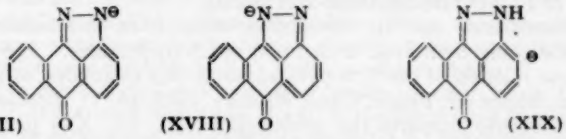
(XVI)

Although pyrazoloanthrone-yellow (XI) is structurally analogous to di*meso*benzanthron-4-yl there are important differences between them. Heating with alkaline dithionite leaves the di*meso*benzanthronyl almost unchanged whilst (XI) dissolves with a deep blue colour. The blue solution contains a salt of the dihydro-derivative (XIV) which is also formed when a suspension of (XI) in aqueous alcoholic sodium hydroxide combines with two atoms of hydrogen in the presence of Raney nickel; no further reduction occurs during longer contact. In contrast, 1 : 9-pyrazoloanthrone takes up one molecule of hydrogen more slowly, forming a greenish-yellow solution.

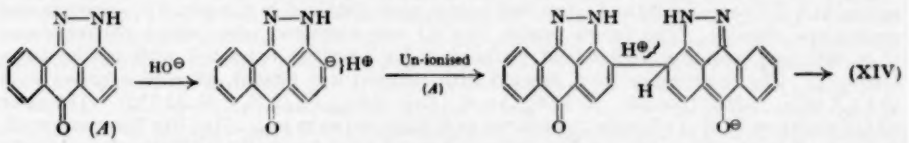
Fusion with alkali hydroxides transforms di*meso*benzanthron-4-yl into violanthrone (Lüttringhaus and Neresheimer, *loc. cit.*), but (XI) undergoes ring-fission with formation of an acid, $C_{28}H_{18}O_4N_4$. The acid regenerates (XI) when heated with sulphuric acid, and for this reason the constitution is probably (XV) or (XVI), the former being preferred for the reason given on p. 1636.

Mechanism of the Self-condensation of 1 : 9-*Pyrazoloanthrone.*—As with *meso*benzanthrone, the self-union of 1 : 9-pyrazoloanthrone requires the use of basic condensing agents, such as alcoholic potassium hydroxide (Bradley and Jadhav, *J.*, 1948, 1622). For

this reason it is probable that the first step in the formation of (XI) is the generation of anions of the reactant, which then condense with undissociated molecules of the same.



The structure of the anion is doubtless intermediate between (XVII), (XVIII), and (XIX), and the importance of the carbanion form may be gauged from the facts that alkylation of potassiopyrrole affords both *C*- and *N*-derivatives (Llubarvin, *Ber.*, 1869, **2**, 101; Bell, *ibid.*, 1878, **11**, 1810; Ciamician and Dennstedt, *ibid.*, 1882, **15**, 2581; Ciamician and Silber, *ibid.*, 1887, **20**, 1369; Ciamician and Zanetti, *ibid.*, 1889, **22**, 659; Zanetti, *ibid.*, p. 2518). Similarly, methyl iodide and the sodium derivative of indole afford 2- and 3- as well as 1-methylindole (Weissgerber, *ibid.*, 1910, **43**, 3521). The self-condensation of 1 : 9-pyrazoloanthrone may then be represented as in the annexed scheme.



That the free NH group of 1 : 9-pyrazoloanthrone is not essential for self-condensation is substantiated by the ready self-condensation of (VII) to (VIII), and by the successful, though less ready, condensation of (IV) to (XIII). In these two instances the basic condensing agent must bring about direct ionisation of nuclear hydrogen as envisaged with *meso*benzanthrone (Bradley and Jadhav, *loc. cit.*), and established by isotopic exchange in the case of *s*-trinitrobenzene (Kharasch, Brown, and McNab, *J. Org. Chem.*, 1937, **2**, 36).

The carbonyl group of 1 : 9-pyrazoloanthrone, however, is necessary for reaction; 1 : 9-5 : 10-dipyrazoloanthracene (X), which lacks a carbonyl group, does not undergo self-condensation in any circumstances.

The occurrence of self-union depends also on the condensing agent; the stronger the base the more facile is the reaction. 1′-Methylpyrazolo(5′ : 4′ : 3′-1 : 13 : 9)anthrone (IV), which is relatively inert, does not undergo self-condensation with alcoholic potassium hydroxide, but does so readily with sodium anilide. Sodium diphenylamide is unable to cause any of the compounds to condense.

Apart from the generation of anions, the self-condensation of 1 : 9-pyrazoloanthrone depends on the occurrence of αβ-unsaturated-ketone characteristics in the nucleus. In this connection the great activity of (VII) should be mentioned, contrasted with the relative inertness of (IV) in which there is no loss of aromatic character from bond-fixation.

A notable feature of the self-union of 1 : 9-pyrazoloanthrone and its *N*-methyl derivatives is the simultaneous formation of 2-anilino-derivatives. The latter result from substitution by anilide anions, and the occurrence of anion-substitution side-by-side with self-union supports the view that self-union, too, is an instance of anion-substitution, the substituting agent being the anion of 1 : 9-pyrazoloanthrone or one of its *N*-methyl derivatives.

A number of related matters may also be mentioned.

3-Bromo-1 : 9-pyrazoloanthrone, heated with alkalis, does not undergo coupling, but only replacement of bromine. The effect may be the result of steric hindrance, but a change in the electrical state of the 2-position resulting from the introduction of a bromine substituent is an equally probable explanation.

Lüttringhaus and Neresheimer (*loc. cit.*) observed that *meso*benzanthrone condensed readily with 3-chloro*meso*benzanthrone in the presence of sodium anilide to form 3 : 4′-di-*meso*benzanthronyl (cf. Bradley and Jadhav, *J.*, 1948, 1623). We have found that the same condensing agent and a mixture of 1 : 9-pyrazoloanthrone and its 2-bromo-derivative

afford only 2-anilino-1 : 9-pyrazoloanthrone. Evidently in the 1 : 9-pyrazoloanthrone series the simple replacement of bromine by anilide anions occurs much more readily than the generation of 1 : 9-pyrazoloanthron-2-yl anions.

1 : 9-Pyrazoloanthrone and its derivatives differ from *meso*benzanthrone and violanthrone in undergoing hydrolysis with fused alkali hydroxides. The effect may be the result of the close relation of the 1 : 9-pyrazoloanthrones to amides, of which they may be regarded as vinylogues (cf. Fuson, *Chem. Reviews*, 1935, **16**, 1; Bradley, *J.*, 1949, 2712). The amide relationship supports the constitutions (II, VI, XV) proposed for the acid products of hydrolysis.

Experimental

Di-(1 : 9-*Pyrazoloanthron-2-yl*).—(*a*) 1 : 9-Pyrazoloanthrone (15 g.), heated with ethyl-alcoholic potassium hydroxide (Mayer and Heil, *Ber.*, 1922, **55**, *B*, 2155), afforded a product (14·5 g.) which, after extraction with acetone, yielded an insoluble residue of di-(1 : 9-pyrazoloanthron-2-yl) (12·5 g.).

(*b*) *N*-Acetyl-2-bromo-1 : 9-pyrazoloanthrone (1 g.) was heated with copper bronze (1 g.) in naphthalene (1 g.) at 250° for 9 hours (G.P. 457,182). The naphthalene was then distilled in steam, and the copper salts and unreacted copper were dissolved in a mixture of ammonia and ammonium chloride. The brown residue (0·5 g.) was extracted with boiling chlorobenzene (2 × 300 c.c.), and the undissolved material (0·3 g.) further extracted with hot pyridine (100 c.c.). The resulting solution, treated with charcoal and filtered, afforded a brown solid (0·1 g.), m. p. >360° (Found : N, 12·6; Ac, 0. Calc. for $C_{28}H_{14}O_2N_4$: N, 12·7%). This gave all the reactions of di-(1 : 9-pyrazoloanthron-2-yl) prepared as in (*a*). Also, like this compound, it dissolved in pyridine with a yellow colour, changed to violet on the addition of methanolic potassium hydroxide.

(*c*) Aniline (" AnalaR "; 60 g.) was heated under reflux. Sodium (2·4 g.), copper bronze (0·1 g.), and nickel oxide (0·1 g.) were added in succession, and the mixture was stirred until hydrogen ceased to be evolved. The temperature was then kept at 40—45° while 1 : 9-pyrazoloanthrone (9 g.) was added, and subsequently raised to 45—60° for 30 minutes. Aniline (30 g.) was added to the viscous product and the stirring continued for 2 hours. After cooling, and addition to dilute hydrochloric acid, the precipitated yellow solid (10 g.) was collected, washed, and dried. Extraction with acetone (Soxhlet) afforded an insoluble residue (5·9 g.) and a solution. The residue was identical with the di-(1 : 9-pyrazoleanthron-2-yl) prepared as in (*a*). The acetone solution afforded brownish-yellow crystals, m. p. 357° (Found : N, 13·2. $C_{20}H_{13}ON_3$ requires N, 13·5%), identical in reactions with the 2-anilino-1 : 9-pyrazoloanthrone prepared from 2-bromo-1 : 9-pyrazoloanthrone and sodium anilide. It dissolved in concentrated sulphuric acid forming a wine-red solution having a faint green fluorescence. Its solution in pyridine was yellow and showed a green fluorescence; on the addition of methanolic potassium hydroxide a wine-red colour and a bright yellow fluorescence developed. It dissolved in 20% aqueous sodium hydroxide forming an orange solution having a green fluorescence; on the addition of sodium dithionite a pale yellow solution and a weak bluish-green fluorescence resulted.

2-*Anilino*-1 : 9-*pyrazoloanthrone*.—A solution of sodium anilide in aniline was prepared from aniline (60 c.c.) as described in (*c*) (above). 2-Bromo-1 : 9-pyrazoloanthrone (4 g.) was added, and the mixture was stirred at 60° for 3 hours. It was then added to dilute hydrochloric acid. The yellowish-brown precipitate was collected, washed, and dried (4 g.; m. p. 324—330°). Recrystallisation from chlorobenzene gave yellowish-brown needles, m. p. 351—352°, not depressed on mixing with the compound, obtained as above.

Action of Copper on N-*Acetyl*-3-*bromo*-1 : 9-*pyrazoloanthrone*.—*N*-Acetyl-3-bromo-1 : 9-pyrazoloanthrone (2 g.), copper bronze (2 g.), and naphthalene (2 g.) at 250° (8 hours) afforded a product from which naphthalene, copper salts, and unchanged copper were then removed. The residue, extracted with alcohol, afforded a product (0·3 g.), m. p. 241—242° (Found : N, 9·9; Br, 2·8%), mainly 1 : 9-pyrazoloanthrone. Further extraction with chlorobenzene also afforded 1 : 9-pyrazoloanthrone, and, finally, extraction with pyridine dissolved a product, m. p. 252—256° (Found : N, 9·6; Br, 16·0%), consisting essentially of 3-bromo-1 : 9-pyrazoloanthrone. There was no evidence for the formation of di-(1 : 9-pyrazoloanthron-3-yl).

A similar result was obtained when anthracene (1 g.) was used instead of naphthalene and the reaction was carried out at 250° for 12 hours.

1 : 9-5 : 10-*Dipyrazoloanthracene*.—This compound (Found : N, 24·3. Calc. for $C_{14}H_8N_4$:

N, 24·6%) resulted in one stage when 1 : 5-dichloroanthraquinone was heated with pyridine and hydrazine hydrate as described by Mohlau (*loc. cit.*). The intermediate 1 : 5-dihydrazinoanthraquinone was not obtained.

1 : 5-Dichloroanthraquinone (10 g.), hydrazine hydrate (10 g.), sodium acetate (10 g.), and pyridine (130 c.c.) gave, after 5 hours at the b. p., 5-chloro-1 : 9-pyrazoloanthrone (m. p. 296—297°; 6 g.) and chlorobenzene-insoluble 1 : 9-5 : 10-dipyrazoloanthracene.

1 : 9-5 : 10-Dipyrazoloanthracene was recovered unaltered after being heated with an excess of a suspension of potassium hydroxide (2·8 g.) in alcohol (2 g.) (6 hours), sodium anilide (4 hours at 40—60°), or precipitated manganese dioxide (1·3 g.), potassium hydroxide (13 g.), and anhydrous potassium acetate (1·3 g.) (30 minutes at 200—250°).

NN-*Diacetyl*-1 : 9-5 : 10-*dipyrazoloanthracene.*—Finely ground 1 : 9-5 : 10-dipyrazoloanthracene dissolved slowly in hot acetic anhydride, forming a blue fluorescent solution. Soon golden-yellow needles began to separate and the fluorescence became yellow. The *diacetyl* derivative which separated from the hot, filtered solution had m. p. 334° [Found : N, 17·7; Ac, 29·4. $C_{14}H_8N_2(O{\cdot}CO{\cdot}CH_3)_2$ requires N, 18·0; Ac, 28·0%].

Dimethyl Derivatives of Di-(1 : 9-*pyrazoloanthron*-2-*yl*).—(*a*) A solution of di-(1 : 9-pyrazoloanthron-2-yl) (4 g.) in water (100 c.c.) and alcohol (100 c.c.) containing sodium hydroxide (10 g.) was stirred at 30—40° while methyl sulphate (10 g.) was added. After 6 hours the product was cooled and set aside for 12 hours, and the precipitated solid collected. This was extracted with ethyl-alcoholic potassium hydroxide, and the residue (2·6 g.) was extracted further with acetone (Soxhlet). A yellow solid, m. p. 336—337°, dissolved, and this was sublimed *in vacuo*. The purified dimethyl derivative (XIII) had m. p. 349° (Found : N, 12·2. Calc. for $C_{30}H_{18}O_2N_4$: N, 12·0%). It dissolved in concentrated sulphuric acid with a reddish-orange colour, and in alkaline sodium dithionite with a bluish-green colour; the original yellow compound separated when the solution was exposed to air.

The acetone-insoluble portion (0·9 g.) of the methylation product did not melt below 360°. It was identical in reactions with the compound formed by the action of ethyl-alcoholic potassium hydroxide on 1′-methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone.

(*b*) 1′-Methylpyrazolo(5′ : 4′ : 3′-1 : 13 : 9)anthrone (3 g.) was stirred for 3 hours at 40—60° with sodium anilide prepared from sodium (1 g.) and aniline (25 g.). The product was cooled and added to dilute hydrochloric acid, and the precipitate collected, washed, and dried. On extraction with acetone deeply coloured solutions formed at first, but later a product dissolved more sparingly and with a pale yellow colour. This was collected separately and isolated in the form of small yellow crystals, m. p. 356—358° (Found : C, 76·6; H, 4·1; N, 11·9. Calc. for $C_{30}H_{18}O_2N_4$: C, 76·9; H, 3·9; N, 12·0%), identical in reactions with the acetone-soluble dimethyl derivative recorded in (*a*).

The deeply coloured acetone extracts formed initially yielded 1·75 g. of a brown solid, m. p. 116—121°, on evaporation. This was dissolved in benzene and chromatographed on alumina. A weakly adsorbed band formed consisting of unchanged 1′-methylpyrazolo(5′ : 4′ : 3′-1 : 13 : 9)-anthrone, but there was also a more strongly adsorbed reddish band. The red product eluted with acetone gave a green-fluorescent yellow solution from which was isolated a yellow compound, m. p. 184—186° (Found : C, 77·4; H, 4·8; N, 12·9. $C_{31}H_{18}ON_2$ requires C, 77·5; H, 4·6; N, 12·9%). It dissolved in concentrated sulphuric acid with a wine-red colour. A red colour developed on addition of methanolic potassium hydroxide to its solution in acetone. The strong colour reaction with alkali indicates that the compound, m. p. 184—186°, is 2-*anilino*-1′-*methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone*. It should be noted also that 4-anilino-1 : 9-pyrazoloanthrone shows only a slight colour change (yellow-orange) when alkali is added to its solution in pyridine (Part I, p. 1634).

(*c*) 1′-Methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone (3 g.) was stirred for 3 hours at 50—60° with sodium anilide prepared from sodium (1 g.) and aniline (30 g.). Even after 10 minutes the colour had changed to deep bluish-green. The product was added to dilute hydrochloric acid, and the brown precipitate collected, dried, and extracted with acetone. A portion dissolved leaving a brown residue (2 g.) of *dimethyl* derivative (VIII), m. p. >360°, unaltered on crystallisation from chlorobenzene (Found : C, 77·2; H, 4·3; N, 12·5%). It dissolved in chlorobenzene to a bluish-red solution, and in alkaline sodium dithionite with a blue colour; aëration of the blue solution afforded a red precipitate.

(*d*) 1′-Methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone (2 g.), heated under reflux with potassium hydroxide (10 g.) and ethyl alcohol (25 c.c.) as described in G.P. 479,284, afforded a product which was then extracted with acetone and chlorobenzene in succession. The reddish-brown residue (0·7 g.) of dimethyl derivative had m. p. >360° (cf. above) (Found : N, 12·1%).

(*e*) 2-Bromo-1′-methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthrone (0·5 g.) was stirred with a solution of sodium dithionite (1 g.) and potassium hydroxide (1 g.) in water (20 c.c.) at 60—80° for 15 minutes. The colour changed gradually from yellow through green to blue. Water was then added, the solution aërated, and the resulting precipitate collected. Extraction with acetone afforded a residue (0·2 g.) having the properties of di-[1′-methylpyrazolo(3′ : 4′ : 5′-1 : 13 : 9)anthron-2-yl].

Action of Potassium Hydroxide and Manganese Dioxide on 1 : 9-*Pyrazoloanthrone. Formation of* 3-o-*Carboxyphenylindazole.*—An intimate mixture of 1 : 9-pyrazoloanthrone (10 g.) and precipitated manganese dioxide (10 g.) was added during 15 minutes to a stirred melt of potassium hydroxide (75 g.) and potassium acetate (7·5 g.) at 200—220°. As the reaction progressed the melt thickened and it was necessary to raise the temperature to 250°. After 30 minutes at 220—250° the product was added to water (1·5 l.), and the suspension was heated for some time at 60° and then filtered. There was a considerable residue, and a deep yellow filtrate which exhibited a green fluorescence. Acidification of the filtrate gave a yellow precipitate, and this was collected, washed, dried (5·6 g.; m. p. 184—186°), and extracted with benzene (Soxhlet). The benzene extract afforded brown crystals (A) (3·6 g.), m. p. 235—246°. Evaporation of the mother-liquor gave 0·8 g. of *acid* which, sublimed *in vacuo*, was obtained as colourless crystals, m. p. 237—238° (Found: C, 69·7; H, 4·6; N, 12·1. $C_{14}H_{10}O_2N_2$ requires C, 70·5; H, 4·2; N, 11·8%), and showed the same reactions as (A). It dissolved in sodium hydrogen carbonate solution with evolution of carbon dioxide. It gave a yellow solution, having a green fluorescence, in concentrated sulphuric acid, and in acetone to a yellow solution which exhibited a blue fluorescence, changed on the addition of potassium hydroxide to a yellow solution with a yellow-green fluorescence.

The acid (A) (0·9 g.) was heated in concentrated sulphuric acid (15 c.c.) at 95—100° for an hour. On addition to water a pale brown precipitate formed. This, collected, washed, and dried, had m. p. 283° and did not depress the m. p. of 1 : 9-pyrazoloanthrone.

The benzene-insoluble portion of the original reaction product was also an acid (0·8 g.). It dissolved in aqueous sodium hydrogen carbonate, and gave a yellow solution in acetone which exhibited a greenish-blue fluorescence; on addition of methyl-alcoholic potassium hydroxide the acetone solution became brownish-yellow and developed a greenish-yellow fluorescence.

Heating (A) with acetic anhydride afforded an *acetyl* derivative, m. p. 217—218° after softening at 189° (Found: C, 68·2; H, 4·4; N, 10·2. $C_{16}H_{12}O_3N_2$ requires C, 68·5; H, 4·3; N, 10·0%).

Action of Potassium Hydroxide and Manganese Dioxide on 1′-*Methylpyrazolo*(5′ : 4′ : 3′-1 : 13 : 9)*anthrone. Formation of* 3-o-*Carboxyphenyl*-1-*methylindazole.*—1′-Methylpyrazolo-(5′ : 4′ : 3′-1 : 13 : 9)anthrone (10 g.) and manganese dioxide (10 g.) were heated with potassium hydroxide (50 g.) and potassium acetate (5 g.) for 10 minutes at 200°, and then for 20 minutes at 220—230°. The alkaline solution obtained on addition to water was filtered and acidified; it afforded 8·4 g. of an *acid*, m. p. 190—194°. Extraction with benzene gave 7·0 g. of brownish-yellow crystals, m. p. 205—206° (Found: N, 11·0. $C_{15}H_{12}O_2N_2$ requires N, 11·1%). There was a considerable residue (B).

The compound, m. p. 205—206°, was easily soluble in aqueous sodium hydrogen carbonate with evolution of carbon dioxide and formation of a yellow solution having a greenish-yellow fluorescence. It gave a yellow solution having a blue fluorescence in acetone, changed to yellow with a yellow-green fluorescence on addition of methanolic potassium hydroxide. It was unchanged by hot acetic anhydride. It depressed the m. p. of 4-hydroxy-1′-methylpyrazolo-(5′ : 4′ : 3′-1 : 13 : 9)anthrone, m. p. 204—205°. When heated with 10 c.c. of concentrated sulphuric acid at 95—100° for an hour 0·7 g. of the acid yielded 0·6 g. of a bright yellow derivative, m. p. 174°. Crystallisation from benzene gave the product in the form of yellow needles, m. p. 185°, shown by colour reactions and mixed m. p. to be 1′-methylpyrazolo-(5′ : 4′ : 3′-1 : 13 : 9)anthrone.

The benzene-insoluble portion (B) of the oxidation product was also an acid (0·85 g.). It did not melt below 360°. It dissolved in aqueous potassium hydrogen carbonate, forming a pale yellow solution with a blue fluorescence. In aqueous potassium hydroxide the solution was yellow with a bright yellowish-green fluorescence.

Action of Fused Potassium Hydroxide on Di-(1 : 9-*pyrazoloanthron*-2-*yl*).—Di-(1 : 9-pyrazolo-anthron-2-yl) (3 g.) was stirred for an hour at 220—250° with potassium hydroxide (30 g.) and potassium acetate (3 g.). The product was added to water, and the suspension was heated and filtered. A yellow filtrate having a green fluorescence was obtained, and this on acidification afforded a gelatinous, brown precipitate. After being washed and dried, the precipitate (1·85 g.)

was extracted with acetone. Evaporation of the extract gave cream-coloured *di*-(3-o-*carboxyphenylindazolin*-7-*yl*) (0·6 g.), m. p. 330—331° (Found: N, 11·5. $C_{28}H_{16}O_4N_4$ requires N, 11·8%). This compound dissolved in aqueous potassium hydrogen carbonate with evolution of carbon dioxide and formation of a yellow solution having a blue fluorescence. A similar solution was obtained in acetone; on addition of methanolic potassium hydroxide the fluorescence became bright yellowish-green. Heating with concentrated sulphuric acid at 90° for an hour reconverted the acid, m. p. 330—331°, into di-(1 : 9-pyrazoloanthron-2-yl).

CLOTHWORKERS RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

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301. *Comparison of the True and the Apparent Dipole Moments of Dissolved Ethers.*

By G. A. BARCLAY and R. J. W. LE FÈVRE.

New measurements together with data in the literature are used to provide ratios between the true and the apparent dipole moments of dimethyl, diethyl, di-*n*- and di-*iso*-propyl, and di-*n*-butyl ethers. The empirical relationships previously suggested for the " solvent effect " cannot be applied with certainty owing to molecular flexibility and consequent doubt concerning the molecular shapes. The types of configuration which could lead to the μ_s^2/μ_g^2 values found by experiment are indicated.

IN this paper we consider the applicability, to five simple aliphatic ethers, of the empirical equations advanced previously (cf. *J.*, 1950, 3370) to relate an apparent dipole moment of a dissolved substance to the true value as determined on the vapour. The present examples were originally selected because the first three members are known to possess Kerr constants which are algebraically negative (Stuart and Volkmann, *Ann. Physik*, 1933, **18**, 121):

	$10^{12}K$ for λ = 5400 Å and press. = 760 mm.
Diemthyl ether	−5 at 18°
Diethyl ,,	−3·9 ,, 62·7°
Di-*n*-propyl ether	−2·3 ,, 123·9°

We have also added the cases of di*iso*propyl and di-*n*-butyl ethers, the Kerr effects for which have not yet been recorded, although for the former at any rate a markedly negative K may be presumed by analogy with di*iso*propyl ketone ($K = -15{\cdot}3 \times 10^{-15}$; Stuart and Volkmann, *loc. cit.*); this aspect is, however, less important now in view of results recently obtained here (cf. *J.*, 1950, 283, 290, 556, 3370).

Since the comparisons sought are those of the orientation polarisations as solutes to those as vapours, it is necessary to ascertain the total polarisations in the two states at one temperature as well as the Debye equations for each ether. Much of this information can be drawn from the literature.

Data providing Polarisations.—We list first (Table 1) a selection of measurements on ethers as gaseous dielectrics, with references in chronological order. Certain earlier and obviously approximate figures are omitted, *e.g.*, those calculated by Højendahl (Thesis, Copenhagen, 1928) from the work of Pohrt (*Ann. Physik*, 1913, **42**, 569). Where an author or combination of authors has made at various times redeterminations on the same substance, only the latest results are quoted, previous papers being noted in parentheses.

For each ether we have investigated the degree of concordance between the various authors by plotting their polarisation values against $1/T$. In the cases where only $(\epsilon - 1)_T$ is given, the appropriate $(P)_T$ has been calculated. The Figure indicates that the agreement is better than might be expected from the Debye equations in Table 1.

By least squares, and from the data used in the Figure, we obtain the relations listed in Table 2. We suggest that this Table summarises the variation of P with T satisfactorily since inspection reveals that for the four homolgous *n*-alkyl ethers there are differences

TABLE 1. *Ethers as gases.*

Results given as	No. of temps.	References
Dimethyl ether		
$(\varepsilon - 1)_T$ values	3	Stuart, *Z. Physik*, 1928, **51**, 490.
$P = 15{\cdot}4 + 10{,}230/T$ ...	4	Sänger, Steiger, and Gächter, *Helv. Phys. Acta*, 1932, **5**, 200 (cf. *ibid.*, 1929, **2**, 130; 1930, **3**, 162).
$P = 15{\cdot}03 + 10{,}130/T$ ...	2	Ramaswamy, *Proc. Indian Acad. Sci.*, 1936, *A*, **4**, 108.
Total Pn.* at each temp.	3	Groves and Sugden, *J.*, 1937, 1779.
Diethyl ether		
$(\varepsilon - 1)_T$ values	4	Stuart, *loc. cit.*
" "	3	Fuchs, *Z. Physik*, 1930, **63**, 824.
$P = 2{\cdot}76 + 7490/T$	4	Sänger, Steiger, and Gächter, *loc. cit.* (cf. also *Physikal. Z.*, 1927, **28**, 455; 1930, **31**, 306).
$P = 23{\cdot}2 + 8620/T$	8	Groves and Sugden, *loc. cit.*
Final μ only	—	Hobbs, Jacokes, and Gross, *Rev. Sci. Instr.*, 1940, **11**, 126.
Total Pn.* at each temp.	7	Moore and Hobbs, *J. Amer. Chem. Soc.*, 1949, **71**, 411.
Di-n-propyl ether		
$P = 41{\cdot}3 + 6350/T$	3	Sänger, Steiger, and Gächter, *loc. cit.*
Total Pn.* at each temp.	3	Groves and Sugden, *loc. cit.*
Diisopropyl ether		
$P = 38{\cdot}5 + 7717{\cdot}8/T$ ...	6	Present work.
Di-n-butyl ether		
Total Pn.* at each temp.	3	Groves and Sugden, *loc. cit.*

* Pn. = polarisation.

of $9{\cdot}2_5$, $10{\cdot}2_5$, and 8·6 c.c. between the successive distortion polarisations—amounts which compare reasonably with the refractivity increases (9·17 and 9·21 c.c., for the D line) from Et_2O to Pr^n_2O to Bu^n_2O (Vogel, *J.*, 1948, 616).

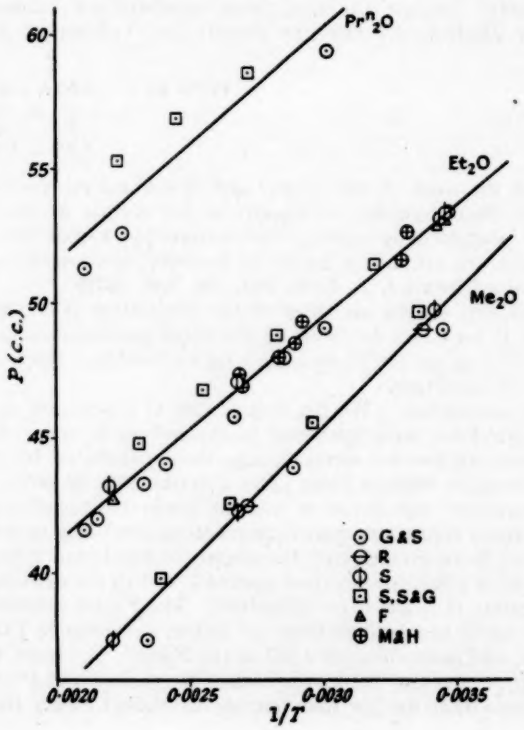


Table 3 presents measurements on the ethers when dissolved in benzene. The total polarisations are those shown by the authors cited, except in the cases of the Chinese paper (where we have deduced 71·7 c.c. from the dielectric constants and density figures given)

TABLE 2.

Me_2O	$(P)_T = 15{\cdot}2 + 10\,080/T$	$\mu = 1{\cdot}29$ D
Et_2O	$(P)_T = 24{\cdot}4_5 + 8340/T$	$\mu = 1{\cdot}17$ D
Pr^n_2O	$(P)_T = 34{\cdot}7 + 8505/T$	$\mu = 1{\cdot}18$ D
Pr^i_2O	$(P)_T = 38{\cdot}5 + 7718/T$	$\mu = 1{\cdot}13$ D
Bu^n_2O	$(P)_T = 43{\cdot}3 + 8303/T$	$\mu = 1{\cdot}16$ D

TABLE 3. *Ethers as solutes in benzene.*

Temp.	No. of solns. examined	Polarisation at infinite dilution (c.c.)	References
Dimethyl ether			
25°	6	47·3	Present work.
Diethyl ether			
20	5	54·8	Lange, *Z. Physik*, 1925, **33**, 169.
25	4	54·5	Williams and Krchma, *J. Amer. Chem. Soc.*, 1927, **49**, 1676.
18	10	56·9	Rolinski, *Physikal Z.*, 1928, **29**, 658.
18	3	57·0	Hassel and Uhl, *Z. physikal. Chem.*, 1930, *B*, **8**, 187 (cf. *Naturwiss.*, 1950, **18**, 247; *Z. Elektrochem.*, 1930, **36**, 735).
18·9	2	57·1	Meyer, *Z. physikal Chem.*, 1930, *B*, **8**, 27.
25	4	(56·6)	Spurr and Zeitlin, *J. Amer. Chem. Soc.*, 1950, **72**, 4832.
25	13	$56{\cdot}9_5$	Present work.
*Di-*n*-propyl ether*			
25	4	(66·8)	Spurr and Zeitlin, *loc. cit.*
25	8	60·8	Present work.
Diisopropyl ether			
25	5	71·3	Thomson, *J.*, 1937, 1056.
25	7	70·9	Present work.
*Di-*n*-butyl ether*			
25	11	74·5	Thomson, *loc. cit.*
25	4	71·7	Li and Pao-Chen Hsü, *J. Chinese Chem. Soc.*, 1926, **13**, 11.
25	4	(73·5)	Spurr and Zeitlin, *loc. cit.*

and each of the results of Spurr and Zeitlin (where we have computed the polarisations from the μ and R quoted). Since with our own measurements we extrapolate the $(\epsilon_{12} - \epsilon_2)/w_1$ and $(d_{12} - d_2)/w_1$ values at each w_1 to $w_1 = 0$, we have re-examined the data of Thomson and of Spurr and Zeitlin in the same manner. For the former, with diisopropyl ether both $(\epsilon_{12} - \epsilon_2)/f_1$ and $(d_{12} - d_2)/f_1$ seem to be invariant with f_1, while with di-*n*-butyl ether this is true only of the density. Thus we find :

	Diisopropyl ether	Di-*n*-butyl ether
f_1 range	0 to 0·177	0 to 0·06
$(\alpha\epsilon_2)/f_1$	2·00	$1{\cdot}051 + 2{\cdot}2f_1$
$(\beta d_2)/f_1$	−0·0273	−0·2551

After adjustment to the basis where $\epsilon^{25}_{C_6H_6} = 2{\cdot}2725$ and $d^{25}_{C_6H_6} = 0{\cdot}87378$, the coefficients at $f_1 = 0$ give—*via* Hedestrand's equation (*Z. physikal. Chem.*, 1929, *B*, **2**, 428)—total polarisations of 70·6 and 67·6 c.c. respectively for the dipropyl and the dibutyl ether. These results are somewhat lower than those listed by Thomson. Similar treatment of the f_1, ϵ, and d figures tabulated by Spurr and Zeitlin leads to abnormally high estimates of ${}_\infty P_1$ (*e.g.*, above 75 c.c. for diethyl ether). In Table 3 the polarisations quoted by the American authors for the three ethers concerned are inserted in parentheses.

Table 4 is included to show that the polarisations observed as dilute solutions in benzene, or as pure liquids, resemble one another closely. From the molecular volumes, V, and the distortion polarisations, ${}_DP$ (Table 2), $(n^{25}_{Eff})^2$ is obtained *via* $(n^{25}_{Eff})^2 = (V + 2\,{}_DP)/(V - {}_DP)$; for comparison the corresponding $(n^{25}_D)^2$ figures are also given (Table 4).

TABLE 4. *Ethers as liquids.*

	ε^{25}	d_4^{25}	${}_TP_{Liq.}$ (c.c.)	$(n_{Eff})^2$	$(n_D^{25})^2$
Et_2O	$4{\cdot}26_5$ [1]	0·708	54·5	2·218	2·086
Pr^n_2O	3·39 [2]	0·744	60·9	2·014	1·900
Pr^i_2O	4·04 [2]	0·720	71·4	2·117	1·863
Bu^n_2O	3·08 [2]	0·766	69·6	2·025	1·950

[1] Le Fèvre, *Trans. Faraday Soc.*, 1938, **34**, 1127. [2] Pyle, *Phys. Rev.*, 1931, ii, **38**, 1057. [3] Thomson, *loc. cit.*

TABLE 5.

	Me_2O	Et_2O	Pr^n_2O	Pr^i_2O	Bu^n_2O
$({}_TP)_{gas}$	49·0	$52{\cdot}4_5$	63·2	64·4	71·2
${}_DP$	15·2	$24{\cdot}4_5$	34·7	38·5	43·3
$({}_oP)_{gas}$	33·8	28·0	28·5	25·9	27·9
$({}_TP_\infty)_{C_6H_6}$	47·3	$56{\cdot}9_5$	60·8	70·9	67·6
$({}_oP_\infty)_{C_6H_6}$	32·1	32·5	26·1	32·4	24·3
μ_g	1·29	1·17	1·18	1·13	1·17
μ_B	1·25	1·26	1·13	1·26	1·09
${}_oP_s/{}_oP_g$	0·950	1·16	0·916	1·25	0·871

Discussion.—In Table 5 we assemble our results under the headings used before (Barclay and Le Fèvre, *J.*, 1950, 556; Angyal, Barclay, and Le Fèvre, *J.*, 1950, 3370).

The ratios forming the bottom line of Table 5 are now to be compared with figures calculated by equations (*a*), (*b*), and (*c*):

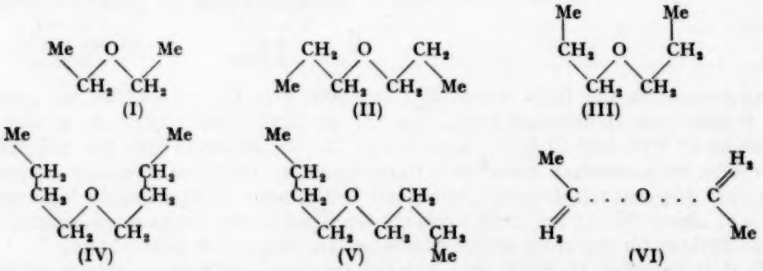
$$ {}_oP_s/{}_oP_g = 1 + k\,[\exp x^2 - (n^2_{Eff})_2/(n^2_{Eff})^2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$ {}_oP_s/{}_oP_g = 1 + k\,[\exp x^2 - \exp (h_2^2 - h_1^2)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

$$ {}_oP_s/{}_oP_g = 1 + k\,[\exp x^2 - \exp (R_1/R_2)\,(1 - A_1B_1C_1/A_2B_2C_2)] \quad . \quad . \quad (c)$$

In these, subscripts 1 or 2 indicate solute or solvent respectively. For benzene at 25°, n^2_{Eff} is 2·300 (from measurements of ${}_TP_{gas}$ by McAlpine and Smyth, *J. Amer. Chem. Soc.*, 1933, **55**, 453, and Ramaswamy, *Proc. Indian Acad. Sci.*, 1936, *A*, **4**, 108), $(n_2^2)_D$ is 2·2417, the volume polarisation (k) is 0·2978 c.c., $[R_2]_D$ is 26·15 c.c., and $A_2B_2C_2$ is 117·6; requisite $[R]_D$ data for the ethers are taken from Vogel (*J.*, 1948, 616); Table 4 gives the relevant figures for $(n^2_{Eff})_1$ and $(n_1^2)_D$; x^2 and h_1^2 or h_2^2 are computed from diagrams incorporating "Wirkungsradien" as described in the papers cited at the head of this section (h_2^2 for benzene is 0·101).

As a basis for the construction of these scale drawings we have used the C–C and C–O interatomic distances and C–O–C angles listed by Allen and Sutton (*loc. cit.*) for dimethyl and diethyl ether. Only in the former case can the molecular shape be foreseen with certainty. For the higher homologues we initially tried an extended zig-zag arrangement (*e.g.*, as I and II), since *X*-ray analyses of long-chain solid aliphatic substances (cf., *e.g.*, Hendricks, *Chem. Reviews*, 1930, **7**, 431) suggested this as a reasonable first guess. However, Table 6 shows it to be unsatisfactory. Estimates, based on models of types such as (III), (IV), or (V), are therefore included for comparison. Good agreement with experiment



is obtained if diethyl ether is given a "*trans*"-disposition of the two methyls about the C–O–C plane (indicated on edge by VI). For di*iso*propyl ether we have taken the H–C–O–C–H arrangement as flat, with the hydrogen atoms close together (*ca.* 1·7 Å between centres).

However, while drawings indicate that these and other modifications are sterically allowable, we recognise the probability that, because of the flexibility of the alkyl radicals, the correct effective molecular shapes are some unknown average of all the possibilities. Such a suggestion is compatible with the information in Table 6, in which the various "calculated" ratios are compared with those "found."

We have pointed out in our previous papers that the usefulness of relation (*a*) for *a priori* computations of μ_{gas} is increased if accessible quantities such as n_D^2 may be employed in place of n^2_{IR} (the evaluation of which implies preknowledge of polarisation–temperature measurements, from which μ_{gas} is directly available, for the gaseous substance). Accordingly we now list (Table 7) the "gas" dipole moments obtained *via* equation (*a*) from determinations with benzene as solvent, using n_D^2 figures from Table 4. It is seen that for each of four of the ethers a configuration (used last where more than one is considered) exists permitting an estimate of μ_{gas} within $\pm 3\%$ of the correct value. With the diethyl, di-*n*-propyl, and di-*n*-butyl members, the ratios $(n^2_{IR})/(n_D^2)$ are all between

TABLE 6.

	A_1	B_1	C_1	R_1	$_0P_e/_0P_g$ calc. *via* eqns. (*a*)	(*b*)	(*c*)	$_0P_e/_0P_g$ found
Me_2O	4·05	6·35	4·00	13·07 *	—	0·98	0·98	0·95
Et_2O (zig-zag)	4·42	8·80	4·00	22·51	0·98	1·00	1·06	1·16
,, (as VI)	4·36	7·20	6·90	,,	1·18	1·20	1·41	,,
Pr^n_2O (zig-zag)	4·42	11·25	4·00	31·68	0·95	1·03	1·16	0·92
,, (as III)	5·95	7·90	4·00	,,	0·88	0·91	1·07	,,
Pr^i_2O	4·30	7·84	6·45	31·71	1·11	1·12	1·33	1·25
Bu^n_2O (zig-zag)	4·42	13·85	4·00	40·89	0·95	1·06	1·24	0·87
,, (as IV)	6·81	10·37	4·00	,,	0·94	1·00	1·25	,,
,, (as V)	8·72	10·50	4·00	,,	0·83	0·95	1·16	,,

* Calc. from Vogel's atomic constants (*loc. cit.*). Lowery's measurements (*Proc. Phys. Soc.*, 1927, **40**, 27) on gaseous dimethyl ether lead to $R_{5461} = 13{\cdot}00$ c.c.

TABLE 7.

Ether	Me_2O	Et_2O	Pr^n_2O	Pr^i_2O	Bu^n_2O
$\mu_{C_6H_6}$	1·25	1·26	1·13	1·26	1·09
(μ_{gas}), calc.	1·26 *	1·28, 1·15	1·17, 1·21	1·23	1·12, 1·12, 1·20
(μ_{gas}), found	1·29	1·17	1·18	1·13	1·17
Error (%)	−2·3	+9·4, −1·7	−0·85, +2·5	+8·8	−4·3, −4·3, +2·6

* Equation (*b*) used, since n_D^2 not available at 25°. The configurations used for calculation of μ_{gas} are those listed in order downwards in Table 6.

1·04 and 1·06 (cf. Table 4); for di*iso*propyl ether, however, the ratio is 1·14. If, in this instance, the "effective" refractive indexes are used, μ_{gas} is calculable as $1{\cdot}19_5$ D, and the error as 5·3—6·2%.

EXPERIMENTAL

Materials, Apparatus, and Methods.—Dimethyl and di-*n*-propyl ethers were prepared from the corresponding alcohols, the former being scrubbed with potassium hydroxide solution and finally dried by passage through a potassium hydroxide tower. Other ethers were purchased. The liquid members were treated with sodium and fractionated immediately before use. The benzene was the frozen-out portion from "AnalaR" grade thiophen-free stock. It was stored over sodium wire. The dielectric constants of solutions have been determined with the apparatus noted previously (*J.*, 1948, 1949; 1949, 333); necessary data are tabulated below under the usual headings (cf. *Trans. Faraday Soc.*, 1950, **46**, 1, for definitions and explanation of extrapolation procedure adopted). For the measurements on gaseous di*iso*propyl ether we have used the circuit shown as Fig. 3 in *J.*, 1950, 276, together with the cell assembly illustrated in *J.*, 1950, 290. The third column of Table 8 reports polarisations computed relatively to carbon dioxide, whose polarisation is taken as invariant with temperature and equal to 7·341 c.c. (cf. *Trans. Faraday Soc.*, 1947, **43**, 374), by the expression :

$$P_{Ether} = 7{\cdot}341\ (\delta C/\rho)^{Ether}_{\rho=0}/(\delta C/\rho)^{CO_2}_{\rho=0}$$

The appropriate standardising equation was :

$$(\delta C/\rho)^{CO_2}_{\rho=0} = 2307{\cdot}4/T - 0{\cdot}054$$

TABLE 8. *Diisopropyl ether as a vapour.*

T (A)	$(\delta C/p)_{p\to 0}$	P (c.c.)	P (calc.)	p range (cm.)	No. of observations
354°	53·3	60·5	60·3	26—66	15
373	49·2	58·9	59·2	14—54	12
384	47·2	58·2	58·6	14—63	16
390	46·9	58·7	58·3	15—61	12
405	44·3	57·6	57·6	13—54	14
432	40·6	56·4	56·4	25—66	11

Whence (by least squares) $P = 38{\cdot}5 + 7717{\cdot}8/T$.

TABLE 9. *Solutions in benzene at 25°.*

$w_1 \times 10^5$	ε_{12}	$\alpha\varepsilon_2$	d_{12}	βd_2
0	2·2725	—	0·87378	—
	Dimethyl ether *			
1112	2·3084	3·23	0·87132	−0·221
2056	2·3387	3·23	0·86921	−0·222
2234	2·3477	3·37	0·86895	−0·216
2765	2·3675	3·44	0·86741	−0·230
4628	2·4364	3·54	0·86314	−0·230
5292	2·4543	3·44	0·86373	−0·190

Whence $(\alpha\varepsilon_2)w_1 = 3{\cdot}19 + 6{\cdot}28w_1$; mean $\beta d_2 = -0{\cdot}218$.

	Diethyl ether *			
11 617	2·2940	1·85	0·87159	−0·188
16 806	2·3047	1·98	0·87057	−0·191
21 118	2·3145	1·99	0·86983	−0·187
27 317	2·3232	1·86	0·86881	−0·182
30 123	2·3299	1·82	0·86821	−0·185
32 607	2·3315	1·81	0·86772	−0·186
34 537	2·3383	1·90	0·86720	−0·190
35 980	2·3413	1·91	0·86709	−0·186
37 168	2·3446	1·94	0·86703	−0·182
40 100	2·3470	1·86	0·86628	−0·187
44 178	2·3547	1·86	0·86565	−0·184
56 849	2·3781	1·86	0·86370	−0·177
128 050	2·5135	1·88	0·85010	−0·183

Whence mean $\alpha\varepsilon_2 = 1{\cdot}88$; mean $\beta d_2 = -0{\cdot}185$.

$w_1 \times 10^5$	ε_{12}	$\alpha\varepsilon_2$	d_{12}	βd_2
0	2·2725	—	0·87378	—
	Di-n-propyl ether			
715·2	2·2804	1·10	0·87266	−0·157
719·8	2·2803	1·08	0·87267	−0·154
1152	2·2844	1·03	0·87198	−0·156
1233	2·2862	1·11	0·87196	−0·148
1581	2·2889	1·04	0·87145	−0·147
2123	2·2952	1·06	0·87063	−0·148
2961	2·3043	1·07	0·86944	−0·147
3194	2·3085	1·13	0·86893	−0·152

Whence mean $\alpha\varepsilon_2 = 1{\cdot}08$; mean $\beta d_2 = -0{\cdot}151$.

	Diisopropyl ether			
1 364	2·2937	1·55	0·87168	−0·154
3 395	2·3254	1·56	0·86809	−0·167$_5$
4 963	2·3499	1·56	0·86544	−0·168
8 554	2·4055	1·55$_5$	0·85995	−0·162
12 668	2·4714	1·57	0·85388	−0·157
15 800	2·5237	1·59	0·84789	−0·164
20 077	2·5957	1·61	0·84188	−0·159

Whence $(\alpha\varepsilon_2)w_1 = 1{\cdot}54 + 0{\cdot}28w_1$; $\Sigma(d_{12} - d_2)/\Sigma w_1 = -0{\cdot}161$.

* The concns. in this case are $w_1 \times 10^6$.

The accuracies of the measurements on solutions may be gauged by applying the rule that the greatest probable error is $3\Sigma r/n\sqrt{n}$, where n is the number of observations made, and Σr is the sum of the differences (irrespective of sign) between the values of $\alpha\varepsilon_2$ and βd_2 from experiment and those obtained by averaging (or, where appropriate, by calculation). The polarisation at infinite dilution in benzene at 25° being given by $M_1p_2(1-\beta) + M_1C\alpha\varepsilon_2$, the variations in $(1-\beta)$ and $\alpha\varepsilon_2$, and hence the maximum error in $({}_TP_\infty)_{C_6H_6}$, may be set out as follows:

	Me_2O	Et_2O	Pr^n_2O	Pr^i_2O
$(1-\beta)$	±0·014	±0·003	±0·004	±0·006
$\alpha\varepsilon_2$	±0·08	±0·04	±0·03	±0·01
Max. error in $({}_TP_\infty)_{C_6H_6}$ (c.c.)	0·9	0·6	0·7	0·4

Reference to Table 5 will show these as *ca.* 2, 1, 1, and 0·5% of the polarisations respectively. The higher uncertainty for dimethyl ether may be due to the difficulties of handling a gaseous solute.

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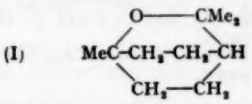
UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, October 6th*, 1951.]

302. *The Effect of Dissolution in Benzene on the Apparent Dipole Moment of* 1 : 8-*Cineole.*

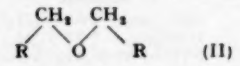
By H. C. Freeman, R. J. W. Le Fèvre, and F. Maramba.

New determinations show $\mu_{gas} = 1{\cdot}58$ D and $\mu_{C_6H_6} = 1{\cdot}57$ D. These values are in agreement with predictions based on two of the empirical formulæ given previously (*J.*, 1950, 3370).

During the preceding measurements, pure specimens of 1 : 8-cineole (I) were being prepared for other work. The constitution of (I) rests on Perkin's synthesis of α-terpineol, and hence of *cis*-terpin from which some cineole may be obtained by dehydration. As constituting a cyclic ether, the component atoms in (I) *must* be mutually "locked," in



(I)



(II)

contradistinction to those in such open-chain (and therefore flexible) species as (II). Accordingly, the molecular shape of (I) seemed predictable with fair certainty from known interatomic distances and valency angles.

Fig. 1. *Side-view of* 1 : 8-*cineole. Dipole axis assumed to bisect oxygen bond angle.*

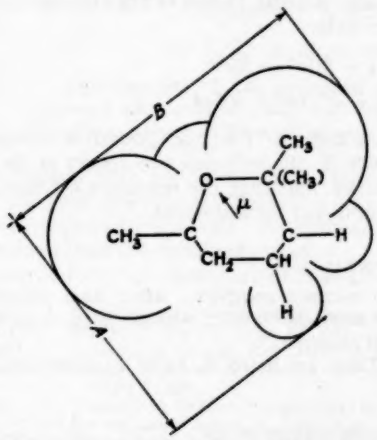
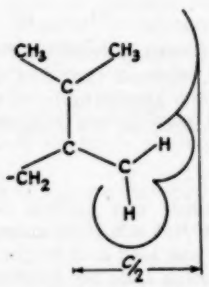


Fig. 2. 1 : 8-*Cineole seen from right-hand end of Fig.* 1, i.e., *along direction of* H–C *and* C–O *bonds.*



Figs. 1 and 2 show different aspects of cineole, drawn (using Stuart's "Wirkungsradien") as described before (*J.*, 1950, 556, 3370). From these we find the dimensions A, B, and C to be related as 6·48 : 8·35 : 6·36, whence $x^2 = -0{\cdot}022$ and $h_1^2 = 0{\cdot}017$. Since (see Experimental section) $(n_1^2)_D^{25}$ is 2·1176 and $[R_L]_D^{Cineole}$ is 45·5 c.c., we can forecast the ratios between the apparent dipole moment, $\mu_{C_6H_6}$, in benzene (appropriate constants for which are in the preceding paper) and the corresponding true value, μ_{gas}, as follow :

By equation	(*a*) (p. 1646)	$\mu^2_{C_6H_6}/\mu^2_{gas}$	= 0·976
,,	(*b*)	,,	= 0·968
,,	(*c*)	,,	= 1·281

Examination of ten solutions (from *ca.* 1 to 6%) yielded a total polarisation of 95·8 c.c. and—*via* the $[R_L]_D$ just quoted—the figure 1·57 D for $\mu_{C_6H_6}$. From this, μ_{gas} should be, by (*a*) 1·59 D, by (*b*) $1{\cdot}59_5$ D, and by (*c*) 1·39 D.

The direct measurement of μ_{gas} was therefore next undertaken, polarisations being read

at seven temperatures between 200° and 300°. The resulting Debye equation, $P = 39{\cdot}5 + 15131/T$, however, displayed an " A " term (39·5 c.c.) which was less than the molecular refraction (45·5 c.c.) of cineole. Distortion polarisations are notoriously difficult to fix precisely. Fortunately this error need not seriously impair the correctness of the moment obtainable from B (= 15131) since μ_{gas} is determined not by the *height* of the P versus $1/T$ line above the $1/T$ axis but only by its slope.

We therefore calculate μ_{gas} as $0{\cdot}01281 \times 15131^{\frac{1}{2}} = 1{\cdot}58$ D—a result which again (cf. previous papers) justifies a preference for equations (*a*) and (*b*) over (*c*).

Two other points may be mentioned briefly : (*a*) The moment now recorded for cineole is some 0·4 D higher than those found for the simple aliphatic ethers. This is reconcilable with the structure (I) since, where comparisons are available, cyclic ethers seem to be more polar than their nearest open-chain relatives :

Substance	Moment	Reference
Ethylene oxide ...	1·89 (gas); 1·83 (C_6H_6)	Angyal, Barclay, and Le Fèvre, *J.*, 1950, 3370.
Dimethyl ether ...	1·29 (gas); 1·25 (C_6H_6)	Previous paper.
Tetrahydrofuran...	1·71—1·83 (C_6H_6–dioxan)	Smyth and Walls, *J. Amer. Chem. Soc.*, 1932, **54**, 3230.
Diethyl ether	1·17 (gas); 1·26 (C_6H_6)	Previous paper.

For the closest analogue to 1 : 8-cineole, *viz.*, diethyl ether, a moment of 1·87 D has been recorded, without experimental details, by Hibbert and Allen (*J. Amer. Chem. Soc.*, 1932, **54**, 4115).

(*b*) We find the dielectric constant of 1 : 8-cineole at 25° to be 4·480 relatively to that of chloroform (for which $\varepsilon = 4{\cdot}724$; cf. Ball, *J.*, 1930, 570). The corresponding density and refractive index (D line) are 0·9209 and 1·4552 respectively. By using these data, the orientation polarisation calculable *via* the Clausius–Mosotti–Debye or the Onsager relation (cf. *J. Amer. Chem. Soc.*, 1936, **58**, 1486) is shown to be

$$_0P = 3M(\varepsilon - n^2)/(\varepsilon + 2)(n^2 + 2)d$$

or

$$_0P = M(\varepsilon - n^2)(2\varepsilon + n^2)/(n^2 + 2)^2\varepsilon d$$

From the former, μ becomes 1·53 D, and from the latter 1·77 D; μ_{gas} (found) is 1·58 D. It is perhaps relevant that Böttcher (*Physica*, 1939, **6**, 59) included two ethers in his wide survey of the applicability of the Onsager equation and that the moments estimated for these were both *ca.* 0·3 D higher than those from direct measurement.

Experimental

1 : 8-Cineole was purified *via* its crystalline *o*-cresol complex; after final distillation (b. p. 173·5°/758 mm.) the material showed $n_D^{18\cdot2}$ 1·4590, $d_D^{18\cdot2}$ 0·9272, whence $[R_L]_D = 45{\cdot}4_8$ c.c. This stock was kept over bright sodium wire until required.

Polarisation Data for Solutions in Benzene.—These are listed in Table 1, under the usual headings (cf. *Trans. Faraday Soc.*, 1950, **46**, 1).

Table 1. 1 : 8-*Cineole in benzene at* 25°.

10^5w_1	ε^{25}	d_4^{25}	$\alpha\varepsilon_2$	βd_2	10^5w_1	ε^{25}	d_4^{25}	$\alpha\varepsilon_2$	βd_2
866	2·2866	0·87444	1·63	0·076	3272	2·3304	0·87484	1·77	0·032
901	2·2871	0·87447	1·62	0·077	3330	2·3295	0·87610	1·71	0·070
1127	2·2932	0·87461	1·75	0·074	4429	2·3522	0·87634	1·80	0·058
1521	2·2987	0·87462	1·72	0·075	5239	2·3646	0·87668	1·76	0·055
1731	2·3023	0·87471	1·72	0·054	6318	2·3881	0·87694	1·83	0·050

whence $(\alpha\varepsilon_2)_{w_1} = 1{\cdot}65 + 2{\cdot}7w_1$

$(\beta d_2)_{w_1} = 0{\cdot}075 - 0{\cdot}46w_1$

and $(_TP)^{25}_{w_1=0} = 95{\cdot}8$ c.c.

Polarisation Data for Cineole as a Vapour.—Essentially the circuits and ancillary equipment depicted in Figs. 1 and 2 of *J.*, 1950, 276 have been used. The b. p. of cineole, however, necessitated new arrangements for heating the replaceable capacity and for observing the pressure of its contents. The former requirement has been adequately met by building a thermostatically controlled oven, the latter less satisfactorily by the insertion of a glass-diaphragm gauge between the cell and an ordinary barometer. Details concerning these items

will be given in a subsequent communication describing the work for which they were particularly developed.

The procedures of measurement and calculation have been set out previously (*Trans. Faraday Soc.*, 1947, **43**, 374). In Table 2, P is the total polarisation at the stated temperature computed relatively to the standardising gas used, namely sulphur dioxide (cf. *J.*, 1950, 276), *i.e.*

$$P^{\text{cineole}} = xP^{SO_2}/x' = (\delta C/\rho)^{\text{cineole}}_{\rho=0}.(10{\cdot}9 + 16160/T)/(\delta C/\rho)^{SO_2}_{\rho=0}$$

TABLE 2.

T (A)	No. of observ-ations	Range (cm. Hg)	x/x'	P (c.c.)	P (calc.)	T (A)	No. of observ-ations	Range (cm. Hg)	x/x'	P (c.c.)	P (calc.)
474·0°	20	19—62	$1{\cdot}59_1$	$71{\cdot}5_8$	$71{\cdot}4_1$	519·1°	13	17—53	$1{\cdot}63_1$	$68{\cdot}5_5$	$68{\cdot}6_4$
490·0	17	18—61	$1{\cdot}60_3$	$70{\cdot}3_4$	$70{\cdot}3_7$	538	19	18—63	$1{\cdot}66_3$	$68{\cdot}0_8$	$67{\cdot}6_1$
493·1	15	20—56	$1{\cdot}60_4$	$70{\cdot}1_3$	$70{\cdot}1_8$	587	16	16—62	$1{\cdot}68_8$	$64{\cdot}9_1$	$65{\cdot}2_7$
509·2	16	20—58	$1{\cdot}63_1$	$69{\cdot}5_9$	$69{\cdot}2_0$						

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UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, October 6th*, 1951.]

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303. *The Apparent Dipole Moments of Water and Hydrogen Sulphide Dissolved in Benzene.*

By C. L. ANGYAL and R. J. W. LE FÈVRE.

Equation (*a*) of the preceding papers has been used to estimate the apparent moments of water and hydrogen sulphide dissolved in benzene. Results are reconcilable with those obtained by direct observation.

IN connection with points raised in the two preceding papers we here comment on the applicability of equation (*a*) (preceding papers) to the cases of water and hydrogen sulphide. Through experimental causes, the moments of these materials are more easily studied in the gaseous than the dissolved states.

Water.—For this substance the following determinations of μ_{gas} are recorded :

1·87	Jona, *Physikal Z.*, 1919, **20**, 14; cf. Zahn, *Phys. Review*, 1926, **27**, 329.
1·82—1·77	Stuart, *Z. Physik*, 1928, **51**, 490.
$1{\cdot}84_7$	Sänger and Steiger, *Helv. Phys. Acta*, 1928, **1**, 369.
$1{\cdot}84_3$	Sänger, *Physikal Z.*, 1930, **31**, 306; cf. also Sänger, Steiger, and Gächter, *Helv. Phys. Acta*, 1932, **5**, 200.
1·83	Stranathan (*Phys. Review*, 1934, **45**, 741.
1·84	Groves and Sugden, *J.*, 1935, 971.
1·831	Stranathan, *Phys. Review*, 1935, **48**, 538.
1·844	Hurdis and Smyth, *J. Amer. Chem. Soc.*, 1942, **64**, 2829.

The 1935 measurements by Stranathan involved 14 temperatures, being in this respect more extensive than any of the others. The Debye equation derived from them is $P = 4{\cdot}03 + 20710/T$, whence $\mu = 1{\cdot}843$ if the various constants listed by Birge (*Reports Progr. Physics*, 1941, **8**, 126) are used. The distortion polarisation, ${}_DP$, is thus about 1·09 times the $[R_L]_D$ (3·71 c.c.).

Since the molecular volume, V, of liquid water at 25° is 18·069 c.c. (" International Critical Tables," Vol. III, p. 25), $(n^2_{Eff})^{H_2O}$ follows, *via* $(V + 2{}_DP)/(V - {}_DP)$, as 1·86. For comparison, $(n^2_D)^{25}$ is 1·7756 (*op. cit.*, Vol. VII, p. 13). The ratio, $(n^2_{Eff})^{C_6H_6}/(n^2_{Eff})^{H_2O}$, is therefore $2{\cdot}30/1{\cdot}86 = 1{\cdot}24$.

A scale drawing, based upon an O–H separation of $0{\cdot}958_4$ Å and an H–O–H angle of 104° 27′ (cf. Herzberg, " Infra-red and Raman Spectra of Polyatomic Molecules," van Nostrand Co., 1945, p. 489) gave $A : B : C$ as $2{\cdot}73 : 3{\cdot}35 : 2{\cdot}44$, and $\exp x^2$ as 0·875.

Accordingly, by equation (*a*) (preceding papers), the apparent dipole moment of water in benzene is predicted as $0{\cdot}944\mu_{gas} = 0{\cdot}944 \times 1{\cdot}84 = 1{\cdot}74$ D.

Actual determinations in this solvent have been reported to show moments of 1·70—1·83 D:

1·70	Williams, *Physikal. Z.*, 1928, **29**, 204, 683.
1·72	*Idem*, *J. Amer. Chem. Soc.*, 1930, **52**, 1838.
1·76	Müller, *Physikal. Z.*, 1934, **35**, 1009.
1·83	Schupp and Mecke, *Z. Elektrochem.*, 1948, **52**, 54.

Williams worked with the saturated solution, the concentration of which he inferred from extant solubility data (Hill, *J. Amer. Chem. Soc.*, 1933, **45**, 1143). Müller, and Schupp and Mecke, examined a number of mixtures, made up by weight, having graded strengths.

We find that the six solutions listed in the paper by Müller and the five in that by Schupp and Mecke form a consistent set when brought to the common basis that $\varepsilon^{20}_{C_6H_6} = 2{\cdot}2825$ and $(d_4^{20})_{C_6H_6} = 0{\cdot}87909$. Thus, with compositions expressed as weight fractions, the ten solutions with $100w_1$ between 0·01141 and 0·05780 show $\alpha\varepsilon_2$ values of 21·0, 19·9, 21·7, 20·7, 20·1, $19{\cdot}7_5$, 19·7, $20{\cdot}0_5$, 20·3, and 20·2 (mean value, 20·3); we neglect the weakest mixture, of $100w_1 = 0{\cdot}0028$, the $\alpha\varepsilon_2$ of which is 25·0. From Müller's experiments it is evident that the average βd_2 is *ca.* $0{\cdot}8_7$, whence $(1 - \beta)$ is only 0·01.

The total polarisation of water at infinite dilution in benzene at 20° is therefore (cf. *Trans. Faraday Soc.*, 1950, **46**, 1) $18{\cdot}0(0{\cdot}341 \times 0{\cdot}01 + 0{\cdot}186 \times 20{\cdot}3) = 68{\cdot}0$ c.c. This, with a distortion polarisation of 4·0 c.c., yields a moment of 1·75 D, in fair agreement with the predicted value of 1·74 D.

If instead of "effective" refractive indexes we use the n_D^2 figures appropriate to water and benzene, equation (*a*) still gives a satisfactory forecast for $\mu_{C_6H_6}$. Since other workers have examined water also in dioxan and ether we include these solvents in the following table:

Solvent	$(\varepsilon_2)^{25}$	$(n_2^2)^{25}_D$	$\mu_{soln.}$ (calc.)	$\mu_{soln.}$ (found)
Benzene	2·2725	2·2417 [1]	1·73	1·75
Dioxan	2·306 [2]	2·0171 [3]	1·77	1·90 [4], 1·89 [5]
Ether	4·250 [1]	1·8295 [1]	1·76	1·71 [4]

[1] *J.*, 1950, 556. [2] *J.*, 1935, 957. [3] *J. Amer. Chem. Soc.*, 1937, **59**, 1344. [4] Linton and Maas, *Canad. J. Res.*, 1932, **7**, 81. [5] Weith, Hobbs, and Gross, *J. Amer. Chem. Soc.*, 1948, **70**, 805.

It is seen that we fail to predict a "positive" solvent effect for dioxan, while the degree of diminution of μ_{gas} for ether is insufficient. The latter, however, is a polar liquid and we have previously noted (*J.*, 1950, 556) that equation (*a*) is inadequate in such cases. Moreover, for both solvents there are possibilities of hydrogen-bonding with the solute which cannot exist in water–benzene mixtures. The factors affecting the apparent moment of water may not therefore be the same throughout the three media listed.

Hydrogen Sulphide.—Two determinations only of μ_{gas} are in the literature:

1·10	Braunmühl, *Physikal. Z.*, 1927, **28**, 141.
0·94	Zahn and Miles, *Phys. Review*, 1928, **32**, 497.

Because of the poor concordance we have re-examined the polarisation–reciprocal temperature relation for this substance.

The apparatus used was that depicted as Figs. 2, 3, and 4 of *J.*, 1950, 276, together with the vapour jacketing arrangement shown in *J.*, 1950, 290. The cell was calibrated with carbon

Polarisations of gaseous hydrogen sulphide.

t (c)	$10^6/T$ (K)	$(\delta C/p)^{H_2S}_{p=0}$	P_{H_2S} (c.c.)	P_{H_2S} (calc.)	p range (cm. Hg)	No. of observations
62·5°	2981°	24·63	26·5	26·3	30—62	11
77·0	2857	22·77	25·6	25·7	30—65	15
81·0	2825	22·61	25·7	25·6	30—67	16
100·0	2681	20·27	24·3	24·9	32—67	14
111·0	2604	20·18	24·9	24·5	31—65	9
132·0	2469	18·42	24·0	23·8	30—67	15
159·0	2315	16·61	23·1	23·1	35—67	15

whence, by least squares, $P = 11{\cdot}88 + 4843{\cdot}7/T$, and $\mu = 0{\cdot}89_2$ D.

dioxide, the temperature-invariant polarisation of which was taken as 7·341 c.c. (cf. Le Fèvre and Russell, *Trans. Faraday Soc.*, 1947, **43**, 374). Since standardising observations showed $(\delta C/p)^{CO_2}_{\gamma\to 0} = 2307{\cdot}4/T - 0{\cdot}054$, the polarisations in the third column of the annexed table are obtained for each temperature by $P_{H_2S} = 7{\cdot}341\ (\delta C/p)^{H_2S}_{\gamma\to 0}/(\delta C/p)^{CO_2}_{\gamma\to 0}$.

Density–temperature values for liquid hydrogen sulphide have been recorded by Steele, McIntosh, and Archibald (*Z. physikal. Chem.*, 1906, **55**, 129). Extrapolation of these gives $d_4^{25} = 0{\cdot}825$, whence the molecular volume, V, at 25°, is 41·3 c.c. As a check on V so obtained, we may note that Bleckrode (*Proc. Roy. Soc.*, 1884, **37**, 339) found n_D to be about 1·38 at room temperatures; $(R_L)_D$ should therefore be approximately $0{\cdot}90 \times 41{\cdot}3/3{\cdot}90 = 9{\cdot}5$ c.c., in fair agreement with 10 c.c. calculated from the refractivities of hydrogen (1·1) and bivalent sulphur (7·8).

Accordingly $(n_{E\infty})^2$ can be estimated from the distortion polarisation, ${}_DP = 11{\cdot}88$ c.c., as 2·211, so that $(n^{C_6H_6}_{E\infty})^2/(n^{H_2S}_{E\infty})^2$ becomes $2{\cdot}300/2{\cdot}211 = 1{\cdot}040$.

From a scale drawing, using a S–H distance of 1·334 Å and an H–S–H angle of 92° 16′ (cf. Herzberg, *op. cit.*, p. 489), the dimensions A, B, and C appear as 3·39, 3·74, and 3·08 respectively. Exp x^2 is therefore 0·867. Equation (*a*) accordingly predits $\mu_{C_6H_6}$ as $0{\cdot}974\mu_{gas}$, *i.e.*, 0·869 D.

An attempt has been made to check this forecast by direct measurement.

After preliminary trials the preparation of mixtures gravimetrically was abandoned in favour of the following procedure (adapted from Bell, *J.*, 1931, 1371): Hydrogen sulphide was bubbled gently through benzene for *ca.* 1 hour; 5·00 c.c. of the resulting solution were then added, at 30°, to a mixture of 0·1N-potassium hydroxide (40·00 c.c.), water (50 c.c.), and neutral 30% hydrogen peroxide solution (2·0 c.c.). After thorough shaking, the superfluous peroxide was destroyed by boiling, and the excess of alkali titrated with 0·1N-hydrochloric acid (methyl-red).

The dielectric constant and density of each solution were recorded as soon as possible after its production. Apparatus and methods have been noted before (*e.g. J.*, 1948, 1949). Bath-temperatures of 30° were necessitated by the season. Loss of gas (bubble formation) proved a nuisance; the following measurements alone are those during which it did not occur:

Hydrogen sulphide in benzene at 30°.

10^5w_1	ϵ^{30}	$\alpha\varepsilon_2$	d_4^{30}	βd_2	10^5w_1	ϵ^{30}	$\alpha\varepsilon_2$	d_4^{30}	βd_2
0	2·2628	—	0·86718	—	732	2·2802	2·37	0·86670	−0·065
245	2·2692	2·61	0·86708	−0·041	972	—	—	0·86653	−0·067
253	2·2682	2·14	0·86708	−0·040	1235	2·2976	2·82	0·86626	−0·074
730	—	—	0·86671	−0·064	1340	—	—	0·86616	−0·076

whence mean $\alpha\varepsilon_2 = 2{\cdot}48_8$ and mean $\beta d_2 = -0{\cdot}061$.

In view of the variations among the $\alpha\varepsilon_2$ factors, the apparently smooth diminution of βd_2 with w_1 may be misleading. Using a mean β of −0·070 with the maximum and minimum values of $\alpha\varepsilon_2$ we estimate total polarisations for hydrogen sulphide of 14·5—18·9 c.c., whence $\mu_{C_6H_6} = 0{\cdot}85$—$0{\cdot}97$ D. The predicted figure (above) is 0·87 D.

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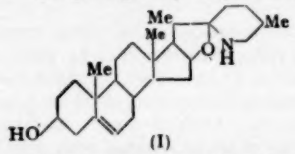
304. Solanum *Alkaloids. Part VII.* The Stereochemical Relationship of Solasodine to Cholesterol.*

By LINDSAY H. BRIGGS and T. O'SHEA.

The preparation of crystalline *N*-acyl derivatives supports the formulation of solasodine as a secondary amine (Part V, *J.*, 1950, 3013). Hydrogenation of " α "- and " β "-solasodan at a platinum oxide catalyst affords " α "- and " β "-dihydrosolasodan, also obtained directly by hydrogenation of solaso-3 : 5-diene with the same catalyst. By applying the method of molecular-rotation differences for correlating the stereochemical configuration in the steroid series solasodine has been shown to have the same stereochemical configuration as cholesterol.

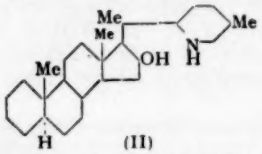
IN Part V (*J.*, 1950, 3013) formula (I) was proposed for solasodine. *N*-Nitroso-derivatives were prepared from solasodine and some of its derivatives, indicating the presence of a secondary amino-group but no crystalline *N*-acyl derivative could be obtained. When the oxide ring had been broken by hydrogenolysis (cf. also Part VI *) *N*-acyl derivatives



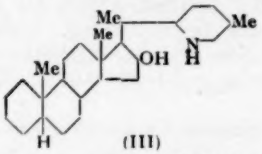
(I)

were readily obtained. This resistance of solasodine towards acylation was attributed to reduced basicity caused by the close association of the nitrogen atom with the oxide ring. By acetylation of solasodine, solasodanol, solaso-3 : 5-diene, and " α "- and " β "-solasodan with acetic anhydride–pyridine, *N*-acetyl derivatives have now been obtained, thus confirming the presence of the secondary amino-group in solasodine. *N*-Benzoyl derivatives, however, could not be prepared.

Hydrogenation of solaso-3 : 5-diene with a palladium–charcoal catalyst affords " α "- and " β "-solasodan as previously reported (Part VI, *loc. cit.*), but by chromatography on alumina the " β "-isomer has now been obtained with a considerably higher melting point. By catalytic hydrogenation of the " α "- and the " β "-isomer with a platinum oxide catalyst " α "- and " β "-dihydrosolasodan have been obtained, with suggested formulæ (II) and (III) respectively, characterised in the case of the " α "-isomer by a diacetyl derivative.



(II)



(III)

Direct hydrogenation of solaso-3 : 5-diene with a platinum oxide catalyst had earlier given the " α "-isomer (Part II, *J.*, 1942, 7) but it was then referred to as hexahydrosolasodiene or dihydro*chano*solasodan, both of which names should be discarded. Fractional crystallisation of the product of this reaction also affords the " β "-isomer in small yield.

Until now there have been too many discrepancies in the reported rotation of solasodine and its derivatives to apply the method of molecular-rotation differences, developed by Barton (Part I, *J.*, 1945, 813, to Part 16, *J. Amer. Chem. Soc.*, 1950, **72**, 1633; for a summary, see Barton and Klyne, *Chem. and Ind.*, 1948, 755), for correlating the stereochemical configuration with that of other steroids. By a systematic study of compounds in this series it has now been shown that solasodine has the same configuration as cholesterol and thus resembles solanidine (cf. Rochelmeyer, *Ber.*, 1938, **71**, 226, and Prelog

* Part VI, *J.*, 1950, 3020.

and Szpilfogel, *Helv. Chim. Acta*, 1944, **27**, 390). Asymmetric centres, additional to those occurring in cholesterol, are present in solasodine at $C_{(16)}$, $C_{(22)}$, and $C_{(25)}$, but no information on the configuration at these points is yet available. Table 1 records the observed molecular rotation and the value calculated from the equation: $[M]_D$ of the solasodine derivative $-[M]_D$ of solasodine (or other standard compound, *e.g.*, dihydrosolasodenol) = $[M]_D$ of the corresponding cholesterol derivative $-[M]_D$ of cholesterol. In the last four compounds the oxide ring has been opened and, for these, dihydrosolasodenol has been taken as a subsidiary standard.

TABLE 1.

Compound	M. p.	$[\alpha]_D$ *	$[M]_D$ (obs.)	$[M]_D$ (calc.) †	$[M]_D$ (obs.) − $[M]_D$ (calc.)
Solasodine	200—202°	−113·5° ± 2°	−469° ± 8°	−469°	Standard
Solasodanol	208—209	− 56·2 ± 3	−234 ± 12	−227	− 7°
Solaso-3 : 5-diene	177—178	−194·9 ± 1·5	−771 ± 6	−773	+ 2
Solasod-4-en-3-one ...	183—184	+ 8·2 ± 1·5	+ 33 ± 6	+ 20	+13
" α "-Solasodan	175—176	− 57·7 ± 3	−231 ± 12	−229	− 2
" β "-Solasodan	159—160	− 56·9 ± 3	−227 ± 12	−227	0
Dihydrosolasodenol ...	261—265	− 65·0 ± 3	−270 ± 12	−270	Standard
Dihydrosolasodanol ...	291—295	− 7·0 ± 4·5	− 29 ± 19	− 28	− 1
" α "-Dihydrosolasodan	184—186	− 8·3 ± 2·5	− 33 ± 10	− 30	− 3
" β "-Dihydrosolasodan	147·5—148·5	− 5·9 ± 3	− 24 ± 12	− 28	+ 4

* All rotations were observed in a 1-dm. micro-tube at room temp. (15—24°). All samples were heated to 120° overnight in a vacuum over magnesium perchlorate, with the exception of solasod-4-en-3-one which was dried at 105°. Chloroform was the solvent throughout, except for the relatively insoluble dihydrosolasodanol where chloroform–alcohol (95 : 5) was employed.

† The values taken for cholesterol and its derivatives are those recorded by Fieser and Fieser, " Natural Products Related to Phenanthrene," Reinhold Publ. Corp., 3rd Edn., pp. 95, 216, 252, 259.

The agreement between the observed and the calculated values is well within the experimental error in almost every case. Since there is no discrepancy in the observed and calculated values for the structures tentatively referred to as " α " and " β " isomers, the configuration assigned to them in Part V (*loc. cit.*) is thus confirmed. The " α "-isomers can therefore be referred to as derivatives of 5α-solasodan and the " β "-isomers as derivatives of 5β-solasodan.

The stereochemical relationship of solasodine with cholesterol has been confirmed with other acyl compounds by somewhat different procedures. *O*-Benzoylsolasodine and *O*-benzoylsolasodanol can be directly correlated by comparing the difference between the benzoyl derivative and the parent compound with the benzoyl derivative and its related parent compound in the cholesterol series as above, and the calculated figures recorded in Table 2 are based on this procedure.

In the case of the acetyl derivatives the procedure is complicated by acetylation of the amino-group. This may be overcome in two ways. First, a constant may be introduced to represent the effect of the *N*-acetyl grouping, *i.e.*, the value, $[M]_D$ of *N*-acetyl-5α-solasodan $- [M]_D$ of 5α-solasodan, is subtracted from the rotation of the solasodine derivative before the effect of acetylation of the 3-hydroxyl group is compared with that in the cholesterol series; *e.g.*, $\{[M]_D$ of diacetylsolasodine $- ([M]_D$ of *N*-acetyl-5α-solasodan $- [M]_D$ of 5α-solasodan$)\} - [M]_D$ of solasodine $= [M]_D$ of cholesteryl acetate $- [M]_D$ of cholesterol, *i.e.*, $[M]_D$ of diacetylsolasodine $+38° - 231° + 469° = -188° + 149°$, or $[M]_D$ of diacetylsolasodine $= -315°$.

In the second method, as an example, *N*-acetyl-5α-solasodan is taken as a standard corresponding to cholestane and the method of molecular rotation differences may be applied to changes in rings A and B: *e.g.* $[M]_D$ of diacetylsolasodine $- [M]_D$ of *N*-acetyl-5α-solasodan $= [M]_D$ of cholesteryl acetate $- [M]_D$ of cholestane, *i.e.*, $[M]_D$ of diacetylsolasodine $+38° = -188° - 91°$ or $[M]_D$ of diacetylsolasodine $= -317°$, in good agreement with the first method. As the second method introduces a smaller number of factors, it has been used to calculate the values recorded in Table 2. A similar standard has to be introduced for the compounds where the oxide ring is broken.

Most of the values obtained are in fair agreement with the calculated values and thus confirm the previous results. The main exception is *N*-acetylsolaso-3 : 5-diene but this

may be ascribed to the " vicinal action " described by Barton and Cox (*Nature*, 1947, **159**, 470) (the compound was purified until it had a constant melting point and rotation).

TABLE 2.

Compound	M. p.	$[\alpha]_D$ *	$[M]_D$ (obs.)	$[M]_D$ (calc.)	$[M]_D$ (obs.) − $[M]_D$ (calc.)
N-Acetyl-5α-solasodan	156—157·5°	− 8·7° ± 4°	− 38° ± 17°	−38°	Standard
N-Acetylsolaso-3 : 5-diene	178—180	−100 ± 2·5	−438 ± 11	−582° ± 17°	+144°
Diacetylsolasodine	165—166·5	− 56 ± 2	−279 ± 10	−317 ± 17	+ 38
Diacetylsolasodanol	186—187	− 13·2 ± 3	− 66 ± 15	− 69 ± 17	+ 3
Diacetyldihydro-5α-solasodan	75—77	+ 39·7 ± 1	+193 ± 5	+193	Standard
Triacetyldihydro-solasodenol	169·5—170·5	− 21·2 ± 4	−115 ± 22	− 86 ± 5	− 29
Triacetyldihydro-solasodanol	156·5—157·5	+ 31·8 ± 2	+173 ± 10	+162 ± 5	+ 11
O-Benzoylsolasodine	220—221	− 80·1 ± 2	−414 ± 10	−394 ± 8	− 20
O-Benzoylsolasodanol	209—211	− 47·2 ± 3	−245 ± 16	−229 ± 12	− 16
Tribenzoyldihydro-solasodenol	228—229	+ 22·5 ± 2	+164 ± 15	—	—

* The rotations and drying of samples were carried out as described for Table 1, except that diacetyldihydro-5α-solasodan was dried at room temperature for 24 hours.

The $[M]_D$ calculated from the rotation recorded for solani-3 : 5-diene (Soltys, *Ber.*, 1933, **66**, 764) (−350°) is also not in agreement with the calculated value (−411°) and thus indicates some " vicinal action " or a compound of doubtful purity.

[*Added, January 14th*, 1952.] On treatment of *N*-nitrosolasodine with boiling aqueous acetic acid, nitrogen is eliminated (cf. Oddo, *Gazzetta*, 1911, **41**, 434; Oddo and Caronna, *Ber.*, 1936, **69**, 283), and on chromatography of the product diosgenin has been isolated in small yield. Since the structure and configuration of diosgenin is known from its conversion into cholesterol (Marker and Turner, *J. Amer. Chem. Soc.*, 1941, **63**, 767), the structure and configuration of solasodine are now also confirmed. The main product of the above reaction is an isomer of diosgenin formed probably by a Demjanow rearrangement during the transformation, details of which will be submitted later.

EXPERIMENTAL

M. p.s were determined in evacuated tubes.

Solasodine.—The final purification of solasodine was carried out by chromatography on alumina, with light petroleum–benzene (3 : 1). Crystallisation of the fraction, m. p. 198—201°, from methyl alcohol afforded hexagonal plates, m. p. 206—202°, $[\alpha]_D^{22}$ −113·5° ± 2° (*c*, 5·03).

Diacetylsolasodine.—A mixture of solasodine (500 mg.), pyridine (5 c.c.), and acetic anhydride (1 c.c., 9 mols.) was heated under reflux for 2 hours and, after cooling, poured on ice plus aqueous ammonia. Successive crystallisation of the precipitated *diacetate* (yield, almost quantitative) from methyl alcohol and ethyl acetate afforded colourless plates, insoluble in dilute acetic acid (Found : C, 75·0; H, 9·4; N, 2·7. $C_{31}H_{47}O_4N$ requires C, 74·8; H, 9·5; N, 2·8%), $[\alpha]_D^{26}$ −56·3° ± 3·5° (*c*, 3·41), −56·2° ± 2° (*c*, 4·90).

O-*Benzoylsolasodine.*—Solasodine (600 mg.) in pyridine (10 c.c.) and benzoyl chloride (0·75 c.c., 4 mols.) were heated under reflux for ½ hour and set aside for 1 day. The precipitate which separated was unchanged solasodine (166 mg.). The filtrate was poured on ice + aqueous ammonia and the product treated with ammonia in acetone. The material recovered on dilution with water, after repeated crystallisation from methyl alcohol and acetone, afforded glistening, colourless, hexagonal plates (Found : C, 78·3; H, 8·9; N, 2·5. Calc. for $C_{34}H_{47}O_3N$: C, 78·9; H, 9·15; N, 2·7%), $[\alpha]_D^{24}$ −80·1° ± 2° (*c*, 5·20), soluble in warm dilute acetic acid. Rochelmeyer (*Arch. Pharm.*, 1939, **277**, 329) records m. p. 216—217° for a benzoyl derivative of solasodine. The benzoyl derivative failed to give a precipitate with digitonin.

Diacetylsolasodanol.—The sample of solasodanol had m. p. 208—209°, $[\alpha]_D^{23}$ −56·2° ± 3° (*c*, 4·97). *Diacetylsolasodanol* was prepared as was acetylsolasodine, from solasodanol (340 mg.), pyridine (8 c.c.), and acetic anhydride (1·4 c.c., 18 mols.). After successive crystallisations from aqueous alcohol, aqueous methyl alcohol, and acetone it separated in colourless plates, insoluble

in dilute acetic acid (Found: C, 74·4; H, 9·8. $C_{31}H_{49}O_4N$ requires C, 74·5; H, 9·9%), $[\alpha]_D^{24}$ −13·2° ± 3° (*c*, 4·16).

Benzoylsolasodanol.—*Benzoylsolasodanol*, prepared similarly to benzoylsolasodine, from solasodanol (200 mg.), pyridine (5 c.c.), and benzoyl chloride (0·5 c.c., 9 mols.), after successive crystallisation from aqueous alcohol, aqueous methyl alcohol, and aqueous acetone, formed hexagonal plates, soluble in warm dilute acetic acid (Found: C, 79·1; H, 9·7; N, 2·4. $C_{34}H_{49}O_3N$ requires C, 78·6; H, 9·5; N, 2·7%), $[\alpha]_D^{22}$ −47·2° ± 3° (*c*, 4·385). It failed to give a precipitate with digitonin.

Dihydrosolasodanol.—A sample of dihydrosolasodanol, purified by Dr. G. A. Nicholls by chromatography on alumina with benzene as the initial solvent and benzene–acetone (1 : 1) for elution, had m. p. 291—295°, $[\alpha]_D^{21}$ −65° ± 2° (*c*, 4·97). The triacetyl derivative, prepared from dihydrosolasodanol (320 mg.), pyridine (4 c.c.), and acetic anhydride (0·5 c.c., 7 mols.) as in the above cases, after repeated crystallisation from aqueous ethyl and methyl alcohol formed plates up to 2 cm. in length, m. p. 156·5—157·5°, slightly higher than that recorded in Part V (*loc. cit.*). It had $[\alpha]_D^{25}$ +31·8° ± 2° (*c*, 6·13) and was insoluble in dilute acetic acid.

Solaso-3 : 5-diene.—The sample of solaso-3 : 5-diene (cf. Part II, *loc. cit.*), after repeated crystallisation from alcohol, methyl alcohol, and acetone, had $[\alpha]_D^{24}$ −194·9° ± 1·5° (*c*, 4·975).

N-*Acetylsolaso-3 : 5-diene.*—This *derivative*, prepared by refluxing solaso-3 : 5-diene (240 mg.), pyridine (5 c.c.), and acetic anhydride (0·5 c.c., 9 mols.) for 2 hours, after repeated crystallisation from acetone and aqueous acetone formed hexagonal plates of constant rotation, $[\alpha]_D^{19}$ 100° ± 2·5° (*c*, 4·27) (Found: C, 79·7; H, 9·8; N, 3·2. $C_{29}H_{43}O_2N$ requires C, 79·6; H, 9·9; N, 3·2%).

No benzoyl derivative could be prepared.

5α-*Solasodan and* 5β-*Solasodan.*—Hydrogenation of solaso-3 : 5-diene in methyl-alcoholic acetic acid as described in Part V (*loc. cit.*) afforded a crude product, m. p. 145—150°, separated readily by crystallisation with methyl alcohol (charcoal) into two main fractions, m. p. 169—175° and m. p. 139—153°. The former was relatively pure and 5α-solasodan was the only product obtained after chromatography (light petroleum; alumina). After crystallisation from acetone it formed shiny flakes, m. p. 175—176°, $[\alpha]_D^{24}$ −58·1° ± 3° (*c*, 5·33), −57·7° ± 2·5° (*c*, 5·19).

The second fraction was refluxed with light petroleum and filtered from an insoluble portion, identified after crystallisation as solasodanol, showing that the original solaso-3 : 5-diene contained some unchanged solasodine. The light petroleum solution was chromatographed on alumina but separation was not clean, the m. p. of the fractions varying from 140—145° to 155—158°. The fraction with the highest m. p., after repeated crystallisation from acetone, formed large needles of " β "-solasodan (5β-solasodan), of constant m. p. 159—160° (Found: C, 80·8; H, 11·1. $C_{27}H_{45}ON$ requires C, 81·1; H, 11·35%), $[\alpha]_D^{23}$ −56·9° ± 3° (*c*, 5·04). At no stage were crystals of the " β "-solasodan, m. p. 132—134°, as recorded in Part V (*loc. cit.*), obtained, and the m. p.s of all the low-melting fractions could be raised above 150° by crystallisation from acetone.

N-*Acetyl-5α-solasodan.*—This *derivative*, prepared by refluxing 5α-solasodan (132 mg.), pyridine (2 c.c.), and acetic anhydride (0·4 c.c., 14 mols.) for 1½ hours, after successive crystallisation from aqueous alcohol, aqueous methyl alcohol, and aqueous acetone, formed hexagonal plates (Found: C, 78·4; H, 10·4; N, 3·1. $C_{29}H_{47}O_2N$ requires C, 78·9; H, 10·7; N, 3·2%), $[\alpha]_D^{24}$ −8·7° ± 4° (*c*, 2·42).

5α-Solasodan could not be benzoylated by the usual method.

N-*Nitroso-5α-solasodan.*—To an ice-cold solution of 5α-solasodan (100 mg.) in glacial acetic acid (1 c.c.) and water (3 c.c.) was added, dropwise and with stirring, a cold solution of sodium nitrite (84 mg., 5 mols.) in water (1 c.c.). The precipitate (quantitative yield), which commenced to form at the first drop, after being kept in the refrigerator overnight, was crystallised successively from 75%, 90%, and 95% alcohol and then formed rods, m. p. 227·5—229° (Found: C, 75·4; H, 10·2; N, 6·3. $C_{27}H_{44}O_2N_2$ requires C, 75·65; H, 10·35; N, 6·5%).

N-*Acetyl-5β-solasodan.*—This *derivative*, prepared by refluxing 5β-solasodan (104 mg.), pyridine (1 c.c.) and acetic anhydride (0·5 c.c., 20 mols.) for 2 hours, after repeated crystallisation from aqueous alcohol and aqueous acetone, formed glistening, hexagonal flakes, m. p. 150·5—151·5° (Found: C, 79·3; H, 10·6; N, 3·1%).

N-*Nitroso-5β-solasodan.*—This *compound*, prepared from 5β-solasodan (95 mg.) in glacial acetic acid (0·25 c.c., 19 mols.) and water (2 c.c.) by a solution of sodium nitrite (90 mg., 5 mols.) in water (1 c.c.), separated after repeated crystallisation from aqueous alcohol and aqueous acetone in colourless needles, m. p. 174—176° (Found: C, 75·95; H, 10·3; N, 6·3%).

Dihydro-5α-solasodan.—5α-Solasodan (110 mg.), in a mixture of glacial acetic acid (10 c.c.)

and acetone (20 c.c.), was hydrogenated in the presence of platinum oxide (75 mg.) at 35 lb./in.² for 40 hours. After removal of the catalyst, the volume was reduced to a few c.c. by vacuum-distillation, and the final solution heated at 100° with excess of ammonia for 20 minutes. The insoluble product, after crystallisation from acetone, formed a mixture of rectangular plates and flattened needles, m. p. 186—188°, undepressed by an authentic sample prepared by hydrogenation of solaso-3 : 5-diene and separated by chromatography on alumina from a light petroleum solution. We are indebted to Dr. G. A. Nicholls for this preparation. Its rotation was $[\alpha]_D^{22}$ −8·3° ± 2·5° (*c*, 5·26).

Diacetyldihydro-5α-solasodan.—Prepared by refluxing dihydro-5α-solasodan (250 mg.), pyridine (5 c.c.), and acetic anhydride (0·6 c.c., 9 mols.) for 2 hours, the *diacetyl* derivative formed colourless flakes after repeated crystallisation from aqueous acetone (Found, in material dried at room temp.: C, 74·5, 74·4; H, 10·3, 10·1; N, 3·2. $C_{31}H_{51}O_3N,H_2O$ requires C, 73·95; H, 10·5; N, 2·8%), $[\alpha]_D^{18}$ +39·7° ± 1° (*c*, 5·47).

Dihydro-5β-solasodan.—5β-Solasodan (70 mg.), in 1 : 2 glacial acetic acid–acetone was hydrogenated in the presence of platinum oxide (70 mg.) at 46 lbs. for 35 hours. After working up of the product as for the 5α-isomer and repeated crystallisation from acetone, the *dihydro*-compound formed plates (Found: C, 81·1, 81·2; H, 11·8, 11·9; N, 3·6. $C_{27}H_{47}ON$ requires C, 80·7; H, 11·8; N, 3·5%), $[\alpha]_D^{20}$ −5·9° ± 3° (*c*, 4·96), m. p. 160·5—161·5°, undepressed by a sample prepared by Dr. G. A. Nicholls by the hydrogenation of solaso-3 : 5-diene with a platinum oxide catalyst (cf. Part II, *loc. cit.*) In the latter case, the 5β-isomer, being somewhat more soluble than the 5α-isomer, was separated by fractionally crystallising the reaction product from acetone.

Dihydrosolasodenol.—A sample of dihydrosolasodenol (Part VI, *loc. cit.*), after purification by chromatography on alumina in acetone–benzene (1 : 9), had $[\alpha]_D^{21}$ −65° ± 3° (*c*, 4·97). Its triacetyl derivative (Part VI, *loc. cit.*) had $[\alpha]_D^{22}$ −21·2° ± 4° (*c*, 2·44).

Tribenzoyldihydrosolasodenol.—This *derivative* was prepared by refluxing dihydrosolasodenol (300 mg.), pyridine (5 c.c.), and benzoyl chloride (1 c.c., 12 mols.) for 30 minutes. The amorphous mauve material finally obtained, after repeated crystallisation from alcohol and aqueous acetone, formed colourless rods, insoluble in dilute acetic acid (Found: C, 78·9; H, 7·9; N, 1·6. $C_{48}H_{57}O_5N$ requires C, 79·2; H, 7·9; N, 1·9%), $[\alpha]_D^{23}$ +22·8° ± 2° (*c*, 5·18), +22·3° ± 2° (*c*, 5·51).

Solasod-4-en-3-one.—A sample prepared by Mr. E. G. Brooker (Part II, *loc. cit.*) and crystallised from acetone formed needles, m. p. 183—184°, $[\alpha]_D^{15}$ +8·2° ± 1·5° (*c*, 5·03).

The analyses are by Dr. T. S. Ma and Mr. A. D. Campbell, Otago University, Dunedin. We are indebted to the Chemical Society, the Australian and New Zealand Association for the Advancement of Science, the Royal Society of New Zealand, and the Research Fund Committee of the University of New Zealand for continued grants.

AUCKLAND UNIVERSITY COLLEGE, AUCKLAND,
NEW ZEALAND.

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305. *The Influence of Structure on the Ultra-violet Absorption Spectra of Heterocyclic Systems. Part II.* Nitrogen Analogues of the Monobenzofluorenes.*

By G. R. CLEMO and D. G. I. FELTON.

The ultra-violet absorption spectra of a series of monobenzofluorenes, monobenzocarbazoles, and their aza-analogues are recorded and compared. The observed band shifts are interpreted in terms of the different activating influences present and the effects which these have in producing extended electronic excitations depending on molecular structure.

IN Part I,* the absorption spectra of a series of indoloquinolines were studied from the point of view of the fusion of an additional benzene ring to the corresponding pyrroloquinolines. As a result of this, the spectra were divided into two series, according as they were modelled on α- or β-naphthylamine. The groups of maxima were not assigned to

* Part I, *J.*, 1951, 671.

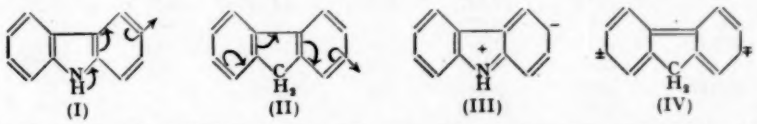
particular modes of excitation and on the evidence available it was not possible to systematise the results further.

Two simple generalisations were quoted from Braude (*Ann. Reports*, 1945, **42**, 128). These were: (*a*) The spectral characteristics of simple heterocyclic systems in which a nitrogen atom is bound to carbon by single bonds, *e.g.*, pyrrole, indole, carbazole, are not appreciably different from those of their carbocyclic analogues containing a methylene group. (*b*) The series in which a nitrogen atom replaces a methine group, *e.g.*, pyridine, quinoline, acridine, show absorptions very similar to those of their aromatic analogues.

The second generalisation appeared to be supported by the closely similar spectra of indolo(2′ : 3′-5 : 6)quinoline and indolo(3′ : 2′-7 : 8)quinoline (Part I*), in which the position of the nitrogen atom in the quinoline ring seems to be of small consequence. Similar support has been adduced from the benzoquinoline (Johnson and Mathews, *J. Amer. Chem. Soc.*, 1944, **66**, 210) and the naphthoquinoline series (Johnson, Woroch and Mathews, *ibid.*, 1947, **69**, 566) and is provided also by the series anthracene, acridine, and phenazine (amongst other papers, cf. Brown and Lahey, *Austral. J. Sci. Res.*, 1950, *A*, **3**, 595) and their benzo-homologues (Badger, Pearce, and Pettit, *J.*, 1951, 3199 *et seq.*).

Further consideration of (*a*) has led us to the conclusion that, theoretically, it is not well based. For, whereas in carbazole the nitrogen atom bears a pair of unshared electrons in a 2*p* orbital, which can coalesce with the π-electrons of the aromatic rings and can thus contribute to the π-electronic state of the molecule as a whole, in fluorene the electrons of the carbon of the methylene group are arranged in tetrahedral sp^3 orbitals and can contribute nothing to the π-electronic distribution, except insofar as they may take part in a hyperconjugative effect. This would be expected to be small in comparison with the polarisation introduced by the hetero-atom in the case of carbazole [Walsh, *Quart. Reviews*, 1948, **2**, 83 (footnote), **84**; for the calculated electron distribution in fluorene and carbazole, see Pullman and Berthier, *Bull. Soc. chim.*, 1948, **15**, 551, and Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87, respectively].

The substitution reactions of carbazole and fluorene are in harmony with this concept. Thus, in carbazole, where the electrons on the nitrogen atom exert the normal directive effect, electrophilic substitution occurs in the order 3, 3 : 6, 1 : 3 : 6, 1 : 3 : 6 : 8 [in agreement with the calculated electron densities (Longuet-Higgins and Coulson, *loc. cit.*)]. In fluorene, on the other hand, the positions of an entering electrophilic group or atom, *e.g.*, NO_2, Br, are 2, 2 : 7; 2 : 4 : 7, etc., where the directive influence on one ring appears to be exercised, not by the methylene group, but by the other aromatic ring (cf. Pullman and Berthier, *loc. cit.*). We may write the polarisation of carbazole as (I) and of fluorene as (II), leading to the quinonoid states (III) and (IV) respectively, among others.



(I) (II) (III) (IV)

In order to test the validity of these rules as applied to fluorene, carbazole, and related compounds leading to the indoloquinolines, we have compared the ultra-violet absorption spectra of compounds of the series (V—XXIII).

The spectra of the following compounds have been taken from the literature: (V) (Mayneord and Roe, *Proc. Roy. Soc.*, 1937, **158**, *A*, 634), (VI) (Menczel, *Z. physikal. Chem.*, 1926, **125**, 195; Pruckner and Witkop, *Annalen*, 1943, **554**, 130), (VIII) (Horner, *ibid.*, 1939, **540**, 73), (IX) (Mayneord and Roe, *loc. cit.*; Orchin and Friedel, *J. Amer. Chem. Soc.*, 1949, **71**, 3002), (XIII) (Orchin and Reggel, *ibid.*, 1948, **70**, 1247; Orchin and Friedel, *loc. cit.*). Spectra of (XII) and (XXIII) have already appeared in Part I (*loc. cit.*).

The spectra of the other members of the series have been determined in ethanolic solution (see Experimental section). Our results for indolo(3′ : 2′-2 : 3)quinoline ("quindoline") (XVIII) agree well with those of Gellert, Raymond-Hamet, and Schlittler (*Helv. Chim. Acta*, 1951, **34**, 642) recorded in connection with the alkaloid cryptolepine.

TABLE 1. *Position of maxima* (mμ); log $\varepsilon_{max.}$ *in parentheses.*

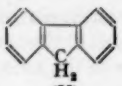
Substance	Group A		Group B		Group C	
V	206	(4·61)	260	(4·28)	290	(3·87)
			264·5	(4·27)	294	(3·81)
					301	(3·98)
VI	243	(4·38)	280	(4·10)	318	(3·47)
	255	(4·08)	286	(4·15)	331	(3·47)
			292	(4·28)		
VII	—	—	267	(4·22)	286	(4·04)
					297	(3·99)
VIII	239	(4·66)	284	(4·40)	340	(3·83)
IX	254	(4·67)	285	(4·10)	316	(4·14)
	263	(4·86)	296	(4·20)	327	(3·36)
			306	(4·18)	345	(3·09)
X	240	(4·44)	280	(4·63)	323	(3·76)
	246	(4·47)	302	(4·29)	338·5	(3·75)
	252	(4·56)	306	(4·30)	355	(3·79)
	258	(4·52)				
XI	259	(4·61)	286	(3·92)	328	(4·0)
	265·5	(4·69)	300	(3·94)	344	(4·15)
			312	(4·01)		
XII	245	(4·48)	292	(4·58)	*ca.* 333 *	(3·55)
XIII	255	(4·71)	286	(4·08)	326	(3·85)
	263	(4·84)	303·5	(4·20)	331	(3·44)
			317	(4·30)	340	(3·85)
XIV	268	(4·81)	317	(4·03)	374	(3·70)
	282	(4·69)	332	(4·13)	394	(3·72)
	292	(4·56)				
XV	259	(4·54)	287	(4·01)	329	(4·19)
	264	(4·60)	301	(3·96)	336·5	(4·08)
	266·5	(4·59)	312	(4·06)	345	(4·30)
			320	(3·99)		
XVI	272	(4·73)	319	(4·13)	372	(3·57)
			334	(4·28)		
XVII	263	(4·64)	313	(3·96)	327·5	(4·26)
					335	(4·16)
					344	(4·44)
XVIII	272	(4·67)	343	(4·25)	385	(3·58)
XIX	269	(4·45)	346	(4·29)	362·5	(4·32)
XX	270	(4·75)	345	(4·25)	396	(3·65)
			355	(4·31)		
XXI	231	(4·68)	302·5	(4·05)	324	(4·10)
	243·5	(4·42)	313	(4·19)	330	(4·06)
	252	(4·20)	—	—	335	(4·19)
XXII	264	(4·67)	316	(4·03)	*ca.* 345 *	(3·70)
	285	(4·00)	326	(4·11)	365	(3·60)
XXIII	245·5	(4·48)	343	(3·98)	—	—
	280	(4·50)				

* Signifies a point of inflexion.

TABLE 2. *Band shifts* (*in* mμ) *on replacement of* $>CH_2$ *by* $>NH$. (+, *bathochromic*; —, *hypsochromic*).

Pair of compounds studied	Group A	Group B	Group C
V—VI	+37	+26; +27·5	+28; +30
VII—VIII	?	+17	+43
IX—X	−2, −5	−5; +6; 0	+7; +11·5; +10
XI—XII	−20·5	−20	−11(?)
XIII—XIV	+5	+13·5; +15	+48; +54
XV—XVI	+5·5	+18; +14	+43
XVII—XVIII	+9	+30	+41
XIX—XX	+1	+9	+33·5
XXI—XXII	+33; +33	+13·5; +13	+21; +30

It will be seen from the series that we have systematically studied the effect on the spectra of the replacement of the methylene group in fluorene and the monobenzofluorenes by >NH, at the same time substituting —N= for a methine group in both the fluorene and carbazole series. There is one omission from the series, that of indeno(3′ : 2′-5 : 6)quinoline,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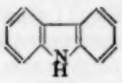
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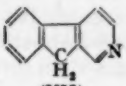
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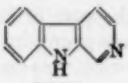
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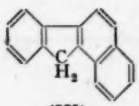
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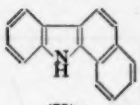
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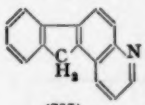
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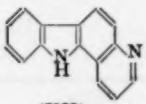
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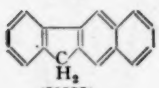
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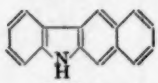
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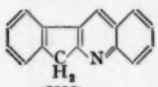
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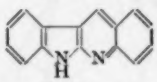
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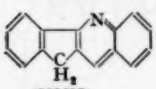
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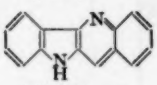
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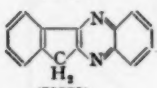
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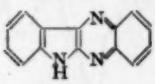
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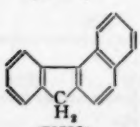
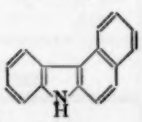

(XXI)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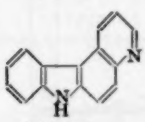
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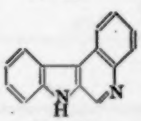

(XXIV)

related to (XXIII). The spectral curves are shown in pairs, demonstrating in each case the effect of replacement of methylene by >NH. Where possible, the effect of replacing a methine group by —N= is shown by the pair of curves immediately above, in order to facilitate comparison.

The maxima are tabulated in Table 1, with values of log $\varepsilon_{max.}$ in parentheses, and are arranged in three groups A, B, and C. These groups are determined by inspection and comparison of curves in each case and are not dependent upon values of log $\varepsilon_{max.}$ (cf. Braude, *loc. cit.*, pp. 123, 128) since these can vary widely as substitution of heterocyclic atoms alters the transition probabilities for each group of bands. (The division of bands into groups may be traced from fluorene throughout the whole series of compounds under examination.)

The influence of structural changes on the position of the groups of bands is shown in Table 2, which lists the band shifts observed on replacement of the methylene group by >NH, and in Table 3, where the effect of replacement of a methine group by a nitrogen

TABLE 3. *Band shifts (in* mμ*) on replacement of* —CH= *by* —N=.

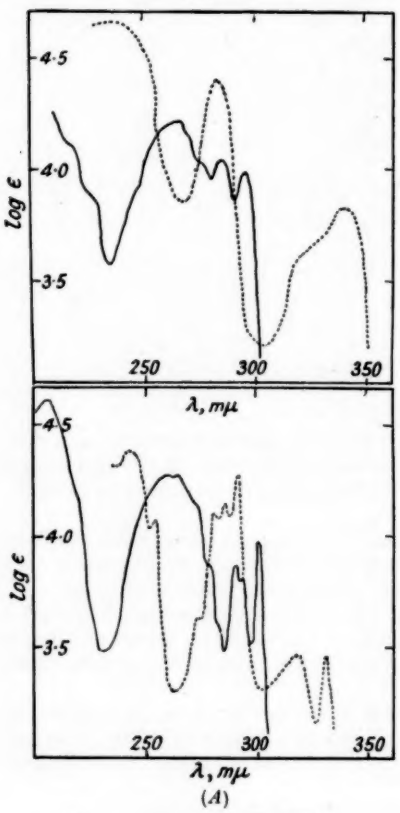
Pair of compounds studied	Group A	Group B	Group C
V—VII	?	+2·5	−4; −4
VI—VIII	−4	−8	+9
IX—XI	+5; +2·5	+1; +4; +6	+12; −1
X—XII	−8	−10(?)	−5(?)
XIII—XV	+4; +3·5	+1; +8·5; +3	+3; +5·5; +5
XIII—XVII	0	+9·5	+1·5; +4; +4
XIII—XIX	+6	+29	+22·5
XIV—XVI	+4	+2; +2	−2
XIV—XVIII	+4	+11	+11
XIV—XX	+2	+28; +23	+22
XXII—XXIII	+24(?)	+17	—

atom in comparable pairs of compounds is tabulated. Where loss of fine structure in a band or group of bands occurs, there has been some dubiety in the comparison of maxima and this is indicated in the tables by a question mark.

Discussion

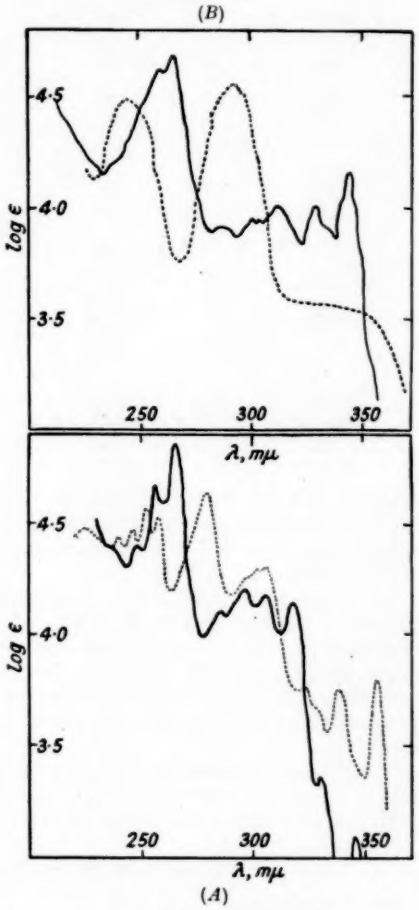
In the case of the fluorene group (V)—(VIII) (Figs. 1*A* and 1*B*), replacement of the methylene group by >NH has led in both cases to pronounced bathochromic shifts, owing to the π-electrons on the nitrogen atom entering into conjugation with those of the aromatic

Fig. 1.



(*A*) ——— *Fluorene* (V).
– – – – – – *Carbazole* (VI).
(*B*) ——— 2-*Azafluorene* (VII.
– – – – – – β-*Carboline* (VIII).

Fig. 2.

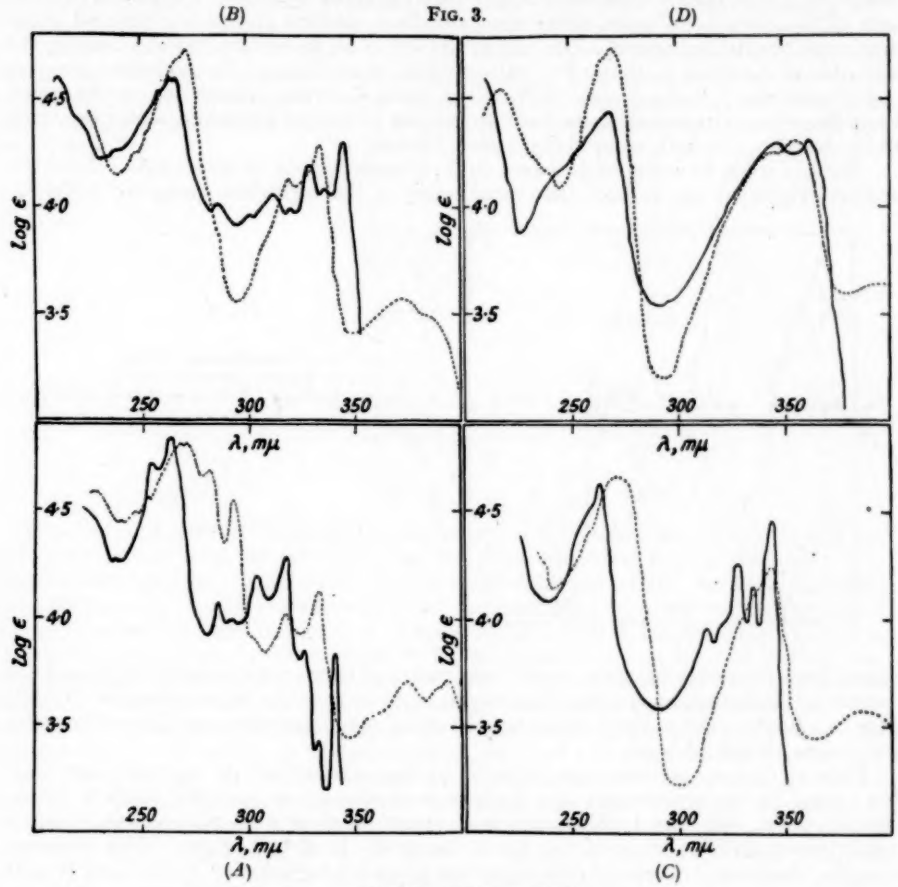


(*A*) ——— 1 : 2-*Benzofluorene* (IX).
– – – – – – 1 : 2-*Benzocarbazole* (X).
(*B*) ——— *Indeno*(2′ : 3′-5 : 6)*quinoline* (XI).
– – – – – – *Indolo*(2′ : 3′-5 : 6)*quinoline* (XII).

rings, so producing a more mobile electronic system. On the other hand, the replacement of a methine group by a nitrogen atom does not add to the number of available mobile electrons and consequently produces very little change in the position of the maxima. Fine structure in individual bands is largely lost, while the intensities in the aza-series tend to be somewhat higher.

In the 1 : 2-benzofluorene group (IX)—(XII) (Figs. 2*A* and 2*B*), replacement of methylene by >NH causes hypsochromic shifts, in some cases very marked, except for the group C maxima of (X). A more profound variation in the envelope shape is noted also in both pairs of spectra. Substitution of —N= for —CH= has produced little effect on the position of the bands in the pair of compounds (IX) and (XI), while increasing the intensities of group C maxima. In the pair of compounds (X) and (XII), hypsochromic shifts occur though there is some doubt about the comparison of the maxima.

FIG. 3.



(*A*) ———— 2 : 3-*Benzofluorene* (XIII).
- - - - - - 2 : 3-*Benzocarbazole* (XIV).
(*B*) ———— *Indeno*(2′ : 3′-2 : 3)*quinoline* (XV).
- - - - - - *Indolo*(2′ : 3′-2 : 3)*quinoline* (XVI).
(*C*) ———— *Indeno*(3′ : 2′-2 : 3)*quinoline* (XVII).
- - - - - - *Indolo*(3′ : 2′-2 : 3)*quinoline* (XVIII).
(*D*) ———— *Indeno*(2′ : 3′-2 : 3)*quinoxaline* (XIX).
- - - - - - *Indolo*(2′ : 3′-2 : 3)*quinoxaline* (XX).

With the linear 2 : 3-benzofluorene group (XIII)—(XX) we are dealing with more than two pairs of analogous compounds, since here we have also studied the effect on the spectra of the position of the aza-atom. In each pair of absorption curves (Figs. 3*A*, 3*B*, and 3*C*) replacement of methylene by >NH had produced a large bathochromic shift, especially in the group C bands, which are shifted by at least 40 mμ in every

case, though the envelope shape is largely retained with loss of fine structure, *i.e.*, the spectra of the carbazole members appear to have been stretched in the direction of longer wave-lengths. In the same three pairs of compounds (XIII)—(XVIII), substitution of —CH= by —N= produces some slight bathochromic shifts and in (XVII) (Fig. 3*C*) a modification of the envelope shape by the virtual extinction of group B maxima. In the two indenoquinolines (XV) and (XVII), this substitution has led to a large increase in the group C intensities, while in the corresponding two indoloquinolines (XVI) and (XVIII) the group B maxima are of higher intensity than the group C bands. The last pair [(XIX) and (XX)] contain the quinoxaline ring, *i.e.*, both methine groups are replaced simultaneously by nitrogen atoms. This causes the loss of all fine structure and a considerable variation in the envelope shape (Fig. 3*D*). Again, replacement of the methylene group by >NH produces a bathochromic shift of the group C bands. Compared to the parent benzofluorene and benzocarbazole, the introduction of the two aza-atoms causes very large shifts (*ca.* 20 mμ) of both group B and group C bands.

The last series of compounds, based on 3 : 4-benzofluorene, is incomplete. From the spectra (Fig. 4) it can be seen that replacement of the methylene group by >NH has

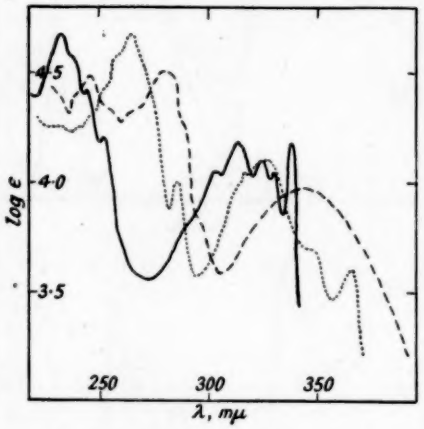


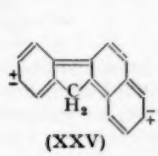
FIG. 4.

——— 3 : 4-*Benzofluorene* (XXI).
– – – – – 3 : 4-*Benzocarbazole* (XXII).
— — — — *Indolo*(3′ : 2′-5 : 6)*quinoline* (XXIII).

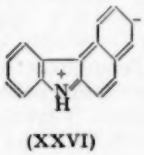
caused large bathochromic shifts of all three groups of bands with considerable loss of fine structure. Introduction of a second nitrogen atom to give the indoloquinoline (XXIII) leads to a further shift to longer wave-lengths and a merging of the group B and C maxima into a wide, ill-defined band.

There is thus an apparent exception to our hypothesis that the greater π-electronic flux caused by the replacement of a fluorene methylene group by >NH leads to bathochromic shifts, *viz.*, the 1 : 2-benzofluorene group, wherein such replacement causes a hypsochromic shift of some of the bands, especially in the aza-series. This apparent exception, however, is a strong point in favour of such a hypothesis. Orchin and Friedel (*loc. cit.*) have pointed out that the spectra of 1 : 2-benzofluorene (IX) and 2 : 3-benzofluorene (XIII) closely resemble each other, while that of 3 : 4-benzofluorene is strikingly distinct, and have attributed this to the close formal resemblance between the latter compound and α-phenylnaphthalene, and the two former structures and β-phenylnaphthalene, respectively. There is a similar pairing in the benzocarbazole series, though in this case it is between the 2 : 3- and the 3 : 4-benzo-isomer, with 1 : 2-benzocarbazole as the exception; the resemblance between the latter pair is not as close as in the benzofluorene series. It may be attributed to a formal relation with β-phenylnaphthylamine, while the 1 : 2-isomer is related to α-phenylnaphthylamine. (In Part I, we attributed the difference in the spectra of individual indoloquinolines and the related pyrroloquinolines to structural analogies with α- and β-naphthylamines.) In the benzofluorene series it is the other aromatic ring which determines the electronic polarisation, apart from some hypercon-

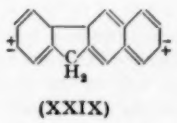
jugative effect of the methylene group. In the benzocarbazole series, however, the main electronic polarisation appears to arise, as predicted, from the lone pair of π electrons on the >NH group; some contribution may be expected from the other aromatic ring as in the benzofluorenes and this may perhaps account for the less close resemblances between the two similar spectra. It is to be expected that electronic polarisations will lead most easily to *p*-quinone like structures in the naphthalenic portion of the molecule. Such *p*-quinonoid structures in the case of carbazole (III) and fluorene (IV) may be invoked to explain the primary electrophilic substitution products of these molecules. Albert, Goldacre, and Phillips (*J.*, 1948, 2240) have suggested a similar increased availability of π electrons for *p*-quinonoid electronic polarisations over the corresponding *o*-quinonoid structures to account for the greatly increased basic strengths of 2- and 5-aminoacridines over the 3- and 4-amino-isomers. Granted such an assumption, we can see that π-electrons will be more available for excitations such as (XXV) and (XXVI), than for (XXVII) and (XXVIII) respectively.



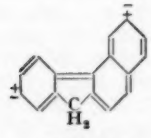
(XXV)



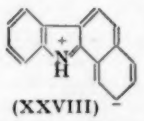
(XXVI)



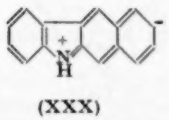
(XXIX)



(XXVII)



(XXVIII)



(XXX)

Thus it will be seen that depending on the source of the π-electrons conjugated with the naphthalenic portion of the structure (*i.e.*, the other benzenoid ring in the case of the benzofluorenes and the >NH group in the benzocarbazole series), the most extended conjugated system will be determined by the angular nature of the compound involved. In the benzofluorene series this is the 1 : 2-benzo-isomer, while in the benzocarbazoles it is the 3 : 4-benzo-compound. Both linear 2 : 3-benzo-isomers are capable of yielding the most extended polarisation, (XXIX) and (XXX). Such extended polarisations lead to "looser" π-electrons, *i.e.*, low-energy excitations, and imply bathochromic shifts. We then see that, the extra electrons introduced by the >NH group being neglected, 1 : 2-benzofluorene should absorb at higher wave-lengths than 1 : 2-benzocarbazole, while the reverse should be true for the 3 : 4-isomers, or, in other words, 1 : 2-benzofluorene should resemble 2 : 3-benzofluorene, while in the benzocarbazole series it should be the 2 : 3- and the 3 : 4-benzo-isomer which should be alike, as in fact is the case. This simple picture is complicated by the bathochromic shift caused by the change from $>CH_2$ to >NH, as exemplified by fluorene and carbazole, but this in addition to the above effect produces the large bathochromic shift, in the case of the 2 : 3- and 3 : 4-benzo-fluorenes and -carbazoles while accounting for the small hypso- and batho-chromic shifts in the 1 : 2-benzo-series.

The band shifts on passing from fluorene to a benzofluorene, and from carbazole to a benzocarbazole are shown in Table 4. The change on annellation is given for each of the possible positions of the additional aromatic residue. It will be seen that, in the fluorene series, bands in groups A and C are moved most for the 1 : 2- and the 2 : 3-isomers (there are unexplained discrepancies in group B bands), while in the carbazole series the larger shifts are seen for the 2 : 3- and the 3 : 4-isomer, for all three groups of bands. In the benzofluorene series the order is brought out well by the shifts of the longest wave-length maximum [see figure in Orchin and Friedel (*loc. cit.*) where this is shown very clearly].

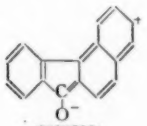
Orchin and Friedel have reported that the spectra of the benzofluorenones show a reversal

in this order, *i.e.*, the 2 : 3- and the 3 : 4-benzo-isomers are similar, while 1 : 2-benzofluorenone is easily distinguishable, and they attribute this to hydrogen bonding in the last case. It seems very probable that our explanation of the difference in the benzocarbazole series is applicable here. Instead of the >NH group with its extra π-electrons

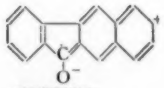
TABLE 4. *Positional effect of annellation on fluorene and carbazole.* (*Band shifts in* mμ.)

Position of additional fused ring	Group A	Group B	Group C
		Fluorene	
1 : 2	+57	+25; +31·5	+26; +33; +44
2 : 3	+57	+26; +39	+36; +37; +39
3 : 4	+25	+42·5; +48·5	+34; +36; +34
		Carbazole	
1 : 2	+ 9; +3	0; +16; +14	+20·5; +24
2 : 3	+25; +27	+31; +40	+56; +63
3 : 4	+21; +30	+30; +34	+27; +34

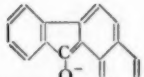
leading to polarisations in a direction different from that in the benzofluorene series, we have the cationoid effect of the carbonyl group causing polarisations in the same direction as in the benzocarbazoles, but in the opposite sense. Thus one would expect electrons to be more readily available for excitations such as (XXXI) and (XXXII) than for (XXXIII).



(XXXI)



(XXXII)



(XXXIII)

Our explanation is supported, not only by the results from the simple benzo-fluorenes and -carbazoles, but also by their aza-analogues. Thus the spectra of (XI) and (XV) resemble each other very closely, with (XVII) as a somewhat modified member of the trio (B bands eclipsed). Likewise, (XVI) and (XXIV) (for spectrum see Part I) are very similar, while (XVIII) and (XXIII), again both very similar, differ somewhat from the former pair by virtue of a bathochromic shift of group B bands. It may be seen from the data for compounds (XVI), (XVIII), (XXIII), and (XXIV) that the position of the aza-atom exerts some effect on the position of band maxima, albeit a small one. This may be attributable to the larger electronegativity of the aza-atom compared with the methine group which it replaces, leading to a clustering of the π-electrons around it, but the effect which this will have on the electronic polarisation is difficult to predict.

In view of the very close similarity between the spectra of (XI) and (XV) (see Table 1), it is worth noting that the structure of (XI) has not been settled unambiguously. Bremer and Hamilton (*J. Amer. Chem. Soc.*, 1951, **73**, 1844) have shown that the Conrad–Limpach synthesis, applied to 2-aminofluorene, yields 4-hydroxyindeno(2′ : 3′-5 : 6)-quinoline and have implied that the Skraup reaction follows the same route. We have attempted to prove this by replacing the hydroxyl group by chlorine and removing this by catalytic hydrogenolysis to yield (XI). However, all attempts to obtain 4-chloroindeno-(2′ : 3′-5 : 6)quinoline have been unsuccessful. Phosphorus oxychloride, alone or with phosphorus pentachloride, has invariably yielded a product containing covalently bound phosphorus, while thionyl chloride, on prolonged refluxing, has given a sulphur-containing product. In view of the well-known tendency for the Skraup reaction to give an angular product, where possible, we consider that (XI) is a reasonable assumption in the absence of contra-indicating fact.

EXPERIMENTAL

The ultra-violet absorption spectra of the compounds studied were determined in ethanolic solution on a Unicam photoelectric spectrophotometer (Model SP 500), in ethanol which was

shown to be optically void in the region under examination. Values of log ε below 3·0 are not plotted since absorption fell off rapidly with increasing wave-length.

2-Azafluorene (VII).—This, m. p. 84—85° (after repeated sublimation at 70°/0·01 mm.), was prepared according to Mills, Palmer, and Tomkinson (*J.*, 1924, **125**, 2365), who give m. p. 78°.

1 : 2-*Benzocarbazole* (X).—Tetrahydro-1 : 2-benzocarbazole (m. p. 139°; Oakeshott and Plant, *J.*, 1928, 1840) (0·75 g.) was heated under reflux with chloranil (1·67 g.) in xylene (50 ml.) for 24 hours and the mixture was worked up in the usual manner (Barclay and Campbell, *J.*, 1945, 530). The product, after crystallisation from aqueous ethanol, was purified by sublimation from a trace of palladised charcoal at 150°/0·01 mm. It formed a white solid, m. p. 227—228°.

Indeno(2′ : 3′-5 : 6)*quinoline* (XI).—This was prepared by a modified Skraup reaction on 2-aminofluorene, with sodium *m*-nitrobenzenesulphonate instead of arsenic acid (Diels and Staehlin, *Ber.*, 1902, **35**, 3275). The product, after crystallisation from light petroleum, was sublimed twice at 120°/0·01 mm., forming a white solid, m. p. 127°, depressed to 103—108° on admixture with 2-aminofluorene, m. p. 127°. Diels and Staehlin gave m. p. 133°.

2 : 3-*Benzocarbazole* (XIV).—Authentic 2 : 3-benzocarbazole, for which we are greatly indebted to Professor J. W. Cook (Glasgow), was resublimed at 280°/0·01 mm., and had m. p. 342°.

Indeno(2′ : 3′-2 : 3)*quinoline* (XV).—*o*-Aminobenzaldehyde (5 g.) and indan-2-one (5·5 g.) were heated under reflux in 2N-hydrochloric acid (65 ml.) for 15 minutes. The brownish-purple hydrochloride was collected and basified with hot dilute sodium hydroxide solution, and the free base collected, dried, and recrystallised successively from ethyl acetate and methanol. After two sublimations (at 130—140°/0·01 mm.) it formed a very pale yellow solid, m. p. 144° (Borsche, *Annalen*, 1937, **532**, 127, gives m. p. 140°) (Found : C, 88·5; H, 5·05. Calc. for $C_{16}H_{11}N$: C, 88·6; H, 5·1%).

Indolo(2′ : 3′-2 : 3)*quinoline* (XVI).—This was prepared following Holt and Petrow (*J.*, 1948, 922) and had m. p. 347° after resublimation.

Indolo(3′ : 2′-2 : 3)*quinoline* (XVIII).—Flavindine [4-carboxyindolo(3′ : 2′-2 : 3)quinoline] was decarboxylated by heating it under reflux with zinc dust in alkaline suspension, and the resulting dihydro-compound, after filtration, was oxidised by a current of air. The product, crystallised from toluene and then sublimed, had m. p. 251—252° (cf. Fichter and Rohner, *Ber.*, 1910, **43**, 3491).

Indeno(2′ : 3′-2 : 3)*quinoxaline* (XIX).—Prepared according to Perkin, Roberts, and Robinson (*J.*, 1912, **101**, 234) and sublimed at 130°/0·01 mm., this formed a pale yellow solid, m. p. 166—167° (lit., 164—165°).

Indolo(2′ : 3′-2 : 3)*quinoxaline* (XX).—This was obtained from isatin and *o*-phenylenediamine, following Schunck and Marchlewski (*Ber.*, 1895, **28**, 2528). After sublimation at atmospheric pressure, it formed long golden-yellow needles, m. p. 286°.

3 : 4-*Benzocarbazole*.—The corresponding tetrahydro-compound (Oakeshott and Plant, *loc. cit.*) was dehydrogenated by chloranil in boiling xylene, and the product, after crystallisation, was sublimed from a little palladised charcoal at 120°/0·01 mm., forming a colourless solid, m. p. 135°.

We thank Professor J. W. Cook, F.R.S., for a sample of 2 : 3-benzocarbazole, and Imperial Chemical Industries Limited, Dyestuffs Division, Blackley, for a gift of flavindine. One of us (D. G. I. F.) thanks the University of Durham for the award of an I.C.I. Fellowship.

UNIVERSITY OF DURHAM, KING'S COLLEGE,
NEWCASTLE-ON-TYNE, 1.

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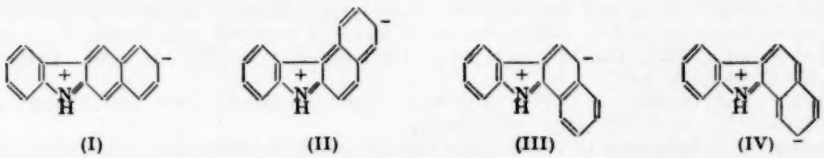
306. *The Influence of Structure on the Ultra-violet Absorption Spectra of Heterocyclic Systems. Part III.* Some Dibenzocarbazoles.*

By D. G. I. Felton.

The explanation advanced in Part II for the absorption spectra of the monobenzocarbazoles is shown to apply to three of the dibenzocarbazole series.

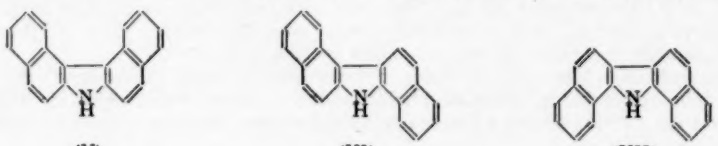
Part II * records a study of the spectra of the three monobenzocarbazoles (amongst other compounds). It was found that the differences observed in both envelope shape and position of maxima could be explained by the interaction of the lone-pair π-electrons on the nitrogen atom with those of the aromatic residues, with some indefinite, but not decisive, contribution from the interaction of the aromatic residues among themselves, as in the benzofluorene series. By using the assumptions that *p*-quinone-type excitations were more probable than *o*-quinonoid excitations and that an extended flux of electrons will be excited more easily by light of lower energy than will a less extended system, it was possible to account for the facts that absorption of light of longer wave-lengths occurred with 2 : 3- and 3 : 4-benzocarbazoles, with the probable transitions (I) and (II), than with 1 : 2-benzocarbazole, where the transition (III), which is more probable than the *o*-quinonoid (IV), is less extended.



(I) (II) (III) (IV)

The same considerations explained the parallels in the spectra of the benzofluorenones and benzocarbazoles and the reversal exhibited in the spectra of both these series of compounds when compared with those of the analogous benzofluorenes (see Part II and Orchin and Friedel, *J. Amer. Chem. Soc.*, 1949, **71**, 3002).

It was desirable, therefore, to test these conclusions further. A closely related series of compounds are the dibenzocarbazoles, three of which (V, VI, and VII) contain the chromo-



(V) (VI) (VII)

phoric systems under investigation arranged in pairs. If the above-mentioned explanation is correct, then (V), which contains two of the extended chromophores of (II), should possess extremely easily excited π-electrons and hence should absorb at longer wave-lengths than (VII), the two chromophores of which are both of the less easily excited type (*i.e.*, III or IV). The analogue (VI), on the other hand, contains a blend of both of the chromophoric types in question and hence may be expected to exhibit facets of both types of spectra, though of less intensity since the probability of a particular transition is less.

The spectra are recorded in Fig. 1 and the values of the absorption maxima (with values of log $\varepsilon_{max.}$ in parentheses) are given in the Table, together with those of the only comparable dibenzofluorene, *i.e.*, 1 : 2-5 : 6-dibenzofluorene, which are available from the literature (Mayneord and Roe, *Proc. Roy. Soc.*, 1937, *A*, **158**, 634). As in Part II, we have classified the bands into three groups, which may be traced from the fluorene spectrum. Those maxima, which are characteristic of the less easily excited transitions and are common to the spectra of (VI) and (VII), are printed in italics. It will be seen that for

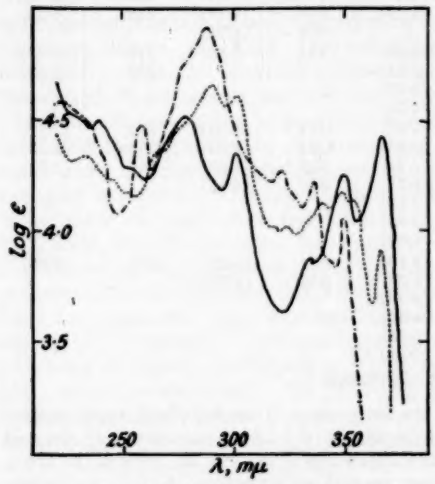
* Part II, preceding paper.

the majority of maxima tabulated, our contention is fully upheld, though there are some bands, *viz.*, those at 240, 252, 280, 335, and 349 mμ, which are common to all three spectra. In the absence of further information, however, we cannot infer that in all three cases it is the same transitions which are concerned.

It is evident from Fig. 2 in which the spectrum of (VI) is compared with the curve obtained by plotting log $\frac{1}{2}[\varepsilon_V + \varepsilon_{VII}]$ against wave-length, so blending the spectra of (V) and (VII) in the simplest possible fashion, that there is a considerable contribution from excitations extending over the molecule as a whole. This molecular contribution is indeterminate in all three cases.

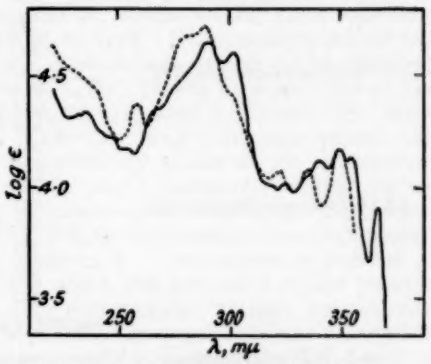
A comparison of the spectra of 1 : 2-5 : 6-dibenzo-fluorene and -carbazole (VI) gives us a further example of the bathochromic shift observed on substituting >NH for $>CH_2$

FIG. 1.



——— 3 : 4-5 : 6-*Dibenzocarbazole* (V).
– – – – – – 1 : 2-5 : 6-*Dibenzocarbazole* (VI).
— · — · — 1 : 2-7 : 8-*Dibenzocarbazole* (VII).

FIG. 2.



——— *Plot of* log ε_{VI} *against* λ.
– – – – – – *Plot of* log $[\frac{1}{2}\varepsilon_V + \frac{1}{2}\varepsilon_{VII}]$ *against* λ.

(cf. fluorene and carbazole, Part II). Since both compounds possess one each of the two types of chromophore residues under consideration, this comparison will be largely unaffected by the dependence of spectral reversal on structure noted for the monobenzofluorenes and -carbazoles. It may be seen that the group A bands (which here are taken as including *all* the short wave-length bands including those which in the fluorene and benzofluorene series occur at too short a wave-length for observation) undergo a bathochromic shift of 40—50 mμ. Group B bands move to longer wave-lengths by about the same amount, while group C bands move by only about 15 mμ. The envelope shape is largely preserved in this comparison.

The family resemblances of the spectral curves of (V), (VI), and (VII), compared to those of the related monobenzocarbazoles, are retained, *e.g.*, the spectrum of (V) shows the virtual disappearance of the group B bands and the characteristic deep minimum (cf. the spectrum of 3 : 4-benzocarbazole, Part II, Fig. 4).

EXPERIMENTAL

The spectra were determined in purified ethanol solutions, with a Unicam photoelectric spectrophotometer (Model SP 500).

3 : 4-5 : 6-Dibenzocarbazole (V) was received from Dr. C. T. Beer as a white solid, m. p. 156° unchanged on resublimation (lit., m. p. 154°, 155°, 157°).

3 : 4-Dihydro-1 : 2-5 : 6-dibenzocarbazole was prepared from 2-naphthylhydrazine hydrochloride (3 g.), sodium acetate (2·1 g.), and 1-tetralone (2·2 ml.), the crude intermediate hydr-

azone being cyclised by heating it with dilute sulphuric acid (14% v/v). On crystallisation from glacial acetic acid, the product formed almost colourless prisms, m. p. 197°. Buu-Hoï, Hoán, and Khôi, of whose paper (*J. Org. Chem.*, 1949, **14**, 492) we were unaware until after the completion of this work, cyclised the hydrazone by means of hydrogen chloride–acetic acid and report m. p. 197°.

1 : 2-5 : 6-*Dibenzocarbazole* (VI).—The above dihydro-compound was heated with palladised charcoal at 250—260° under nitrogen for 2 hours. The mass was extracted with hot benzene, and the solution, after filtration, was evaporated to dryness. The residue, purified by sublimation from a trace of palladised charcoal at 200°/0·1 mm., yielded a very pale yellow solid, m. p. 237° (Buu-Hoï *et al.* give m. p. 237—238°).

Values of $\lambda_{max.}$ *(in* mμ*), with the corresponding values of log* $\varepsilon_{max.}$ *in parentheses.*

Substance	Group A		Group B		Group C	
1 : 2-5 : 6-Dibenzofluorene	248	(4·71)	276	(4·09)	333	(4·30)
	255	(4·77)	285	(4·10)	349	(4·32)
			294	(4·09)		
3 : 4-5 : 6-Dibenzocarbazole (V)	240	(4·50)	334	(3·88)	349	(4·25)
	252 *	(4·28)			366	(4·43)
	279	(4·52)				
	301	(4·35)				
1 : 2-5 : 6-Dibenzocarbazole (VI)	235	(4·33)	318 *	(4·01)	*349*	*(4·17)*
	246 *	(4·23)	*324*	*(4·01)*	354·5	(4·13)
	252 *	*(4·17)*	*335* *	(4·05)	366	(3·91)
	268 *	(4·35)	340	(4·12)		
	280 *	*(4·50)*				
	290	*(4·65)*				
	302	(4·60)				
1 : 2-7 : 8-Dibenzocarbazole (VII)	222	(4·58)	*321*	*(4·27)*	*349*	*(4·06)*
	240 *	(4·35)	*335*	*(4·22)*		
	252 *	*(4·12)*				
	259	(4·48)				
	280 *	*(4·78)*				
	289	*(4·92)*				

* Signifies a point of inflexion.

1 : 2-7 : 8-*Dibenzocarbazole*.—When prepared similarly from 1-naphthylhydrazine hydrochloride (3 g.) and 1-tetralone (2·2 ml.), 3 : 4-dihydro-1 : 2-7 : 8-dibenzocarbazole formed colourless prisms (from dilute acetic acid), m. p. 184° (Buu-Hoï *et al.*, *loc. cit.*, give m. p. 178°). Dehydrogenation was effected as for (VI). After several sublimations, 1 : 2-7 : 8-dibenzocarbazole formed a nearly colourless solid, m. p. 221—222° (lit., m. p. 216°; Buu-Hoï *et al.*, *loc. cit.*, give m. p. 212°, though this may be a misprint).

The author thanks Dr. C. T. Beer for the gift of a sample of 3 : 4-5 : 6-dibenzocarbazole and gratefully acknowledges the award of an I.C.I. Fellowship by the University of Durham. He is warmly indebted to Professor G. R. Clemo, F.R.S., for his interest in this work.

KING'S COLLEGE, UNIVERSITY OF DURHAM,
NEWCASTLE-ON-TYNE, 1.

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307. *The Chemistry of Bivalent Germanium Compounds. Part II.* Some Complex Compounds of Bivalent Germanium.*

By D. A. EVEREST.

The following new complex compounds of bivalent germanium have been prepared: $GeI_2,2NH_2Me$; $Ge(H_2PO_2)_2,GeCl_2$; $3Ge(H_2PO_2)_2,GeBr_2$. They resemble the corresponding tin compounds. Germanium dioxide, in contrast to stannic hydroxide, is reduced to the bivalent state when heated alone with hypophosphorous acid.

THE best-defined complexes of bivalent germanium which were known at the start of this work were of the type $MGeX_3$, where M was a univalent cation, and X was chlorine, bromine, or iodine (Tchakarian, *Compt. rend.*, 1931, **192**, 233; Karantassis and Capatos,

* *J.*, 1950, 2282, is regarded as Part I of this series.

ibid., 1934, **199**, 64; 1935, **201**, 74). Transport experiments (Tchakarian, *ibid.*, 1937, **204**, 117), supported by observations of Raman spectra (Tchakarian, Volkringer, and Freymann, *ibid.*, 1934, **199**, 292; Tchakarian and Volkringer, *ibid.*, 1935, **200**, 1758), showed that in halogen acids bivalent germanium was present as complex anions, *e.g.*, $GeCl_3^-$. It is noteworthy that there is no evidence for the existence of the simple Ge^{++} ion in solution. The existence in hydrochloric acid solution of a complex tartrate of bivalent germanium has also been reported by Robinson (*Ann. Reports*, 1944, **41**, 112).

Germanous Iodide–Methylamine System.—Since bivalent germanium only formed stable solutions in an excess of acid it was considered that complex formation would be more readily observable if the complexing agent was added under anhydrous conditions. In preliminary experiments gaseous ammonia was used as complexing agent, being allowed to react with solid germanous iodide. The pressure–composition curves obtained were irregular and not reproducible, possibly owing to ammonolysis. Reaction readily occurred when germanous iodide was treated with liquid ammonia, germanous imide being formed (Johnson, Morey, and Kott, *J. Amer. Chem. Soc.*, 1932, **54**, 4278). It has been pointed out by Fernelius and Bowman (*Chem. Reviews*, 1940, **26**, 6) that for any given substance the extent of aminolysis was less than that of ammonolysis. Gaseous methylamine was therefore chosen as the complexing agent; the pressure–composition curves obtained indicated the formation of the compound $GeI_2,2NH_2Me$. It was observed that as the solid phase approached the composition GeI_2,NH_2Me it became bright red, the colour reaching maximum intensity at that point. When this composition was passed, the solid phase changed from red to yellow, and was entirely yellow at the composition $GeI_2,2NH_2Me$. There was, however, no break in the pressure–composition curves corresponding to a compound GeI_2,NH_2Me. This may have been due to the dissociation-pressure difference between $GeI_2,2NH_2Me$ and GeI_2,NH_2Me being so small (less than 5 mm.) that the apparatus used was too insensitive to detect it. The maximum pressure of methylamine measured in these experiments was about 200 mm. so that the possible existence of higher methylamine compounds, with a dissociation pressure greater than this, cannot be ruled out. $GeI_2,2NH_2Me$ was insoluble in most solvents but dissolved in hydrochloric acid after the momentary formation of a bright red solid, possibly GeI_2,NH_2Me. When heated, $GeI_2,2NH_2Me$ decomposed in the range 190—200°; when warmed with aqueous sodium hydroxide, it evolved methylamine; with water hydrolysis took place according to the equation:

$$GeI_2,2NH_2Me + 2H_2O = Ge(OH)_2 + 2NH_3MeI$$

Repetition of these experiments with stannous halides and methylamine indicated the formation of $SnI_2,2NH_2Me$ and $SnCl_2,2NH_2Me$ analogous to $GeI_2,2NH_2Me$; the pressure–composition curves also indicated the existence of the monomethylamine compounds SnI_2,NH_2Me and $SnCl_2,NH_2Me$ (Everest, Thesis, London, 1949).

Compounds of Germanous Hypophosphite and Germanous Halides.—Two compounds have been prepared: $Ge(H_2PO_2)_2,GeCl_2$ and $3Ge(H_2PO_2)_2,GeBr_2$, the latter being the less soluble. These were the only compounds isolated, whatever the relative proportions of the hypophosphorous and halogen acids. The compounds were fairly stable in air but were hydrolysed by water, giving germanous hydroxide. Warm concentrated sulphuric and nitric acids rapidly decomposed them, giving germanium dioxide. They dissolved in concentrated halogen acids, hypophosphorous or phosphoric acid, the last two being new solvents for bivalent germanium compounds. Both $Ge(H_2PO_2)_2,GeCl_2$ and $3Ge(H_2PO_2)_2,GeBr_2$ had sharp melting points (124° and 129° respectively); no other germanous compound has been reported to have a melting point with the exception of germanous bromide (m. p. 122°) (Brewer and Dennis, *J. Phys. Chem.*, 1927, **31**, 1526). The reported properties of germanous bromide were exceptional (*e.g.*, it was soluble in alcohol and acetone) and differed sharply from those of the other germanous halides. $Ge(H_2PO_2)_2,GeCl_2$ and $3Ge(H_2PO_2)_2,GeBr_2$ resembled the corresponding bivalent tin compounds (Everest, *J.*, 1951, 2903) in their reactions, in possessing analogous formulæ, and in having sharp melting points. This possibly indicated that these compounds had similar structures.

If germanium dioxide was heated alone with hypophosphorous acid it was dissolved to give a clear yellowish-green solution which gave the reactions of bivalent germanium, reduction having occurred. This behaviour was in contrast to that of stannic hydroxide, which, although soluble in hypophosphorous acid, was not reduced to the bivalent state in absence of hydrochloric acid (Everest, *loc. cit.*).

Experimental

Germanous Iodide–Methylamine System.—Germanous iodide was prepared by the method of Powell and Brewer (*J.*, 1938, 197) and carefully dried before use. Methylamine was prepared by heating methylamine hydrochloride with calcium oxide and condensing the methylamine in a freezing mixture. It was then dried over metallic sodium. The pressure–composition curves were followed by adding gaseous methylamine to germanous iodide in successive small portions, allowing 24—36 hours for the system to attain equilibrium, and measuring the vapour pressure of methylamine. The amount of methylamine absorbed was followed by weighing the reaction mixture. The apparatus used was based on that described by Hart and Partington (*J.*, 1943, 104), and was kept in a thermostat within $\pm 0{\cdot}1°$. The vapour pressure of methylamine over $GeI_2,2NH_2Me$ was 7 mm. at 25° and 15 mm. at 75°.

Analytical Procedures.—Germanium. After reduction to the bivalent state by an excess of boiling hypophosphorous acid and 6N-hydrochloric acid for 30 minutes, the cooled solution was titrated in an inert atmosphere with 0·1N-iodine (standardised with pure germanium dioxide). The end-point was sharp but slowly faded, the germanium values obtained tending to be higher than the theoretical.

Halogens. The sample was dissolved in aqueous sodium hydroxide in presence of hydrogen peroxide and heated for 2 hours to oxidise the hypophosphite. Halogens were then precipitated with silver nitrate.

Phosphorus. The sample was dissolved in 6N-hydrochloric acid in presence of the minimum amount of hydrogen peroxide needed to oxidise the germanium to the quadrivalent state. The germanium was then precipitated as disulphide and removed. The solution was then treated with bromine to oxidise the hypophosphite to phosphate and, after evaporation nearly to dryness to drive off all the hydrochloric acid, the phosphate was determined gravimetrically with ammonium molybdate.

Double Salt, $Ge(H_2PO_2)_2,GeCl_2$.—This *salt* (m. p. 124°) was prepared by heating activated germanium dioxide (0·5 g.), formed by dissolving the normal oxide in alkali and reprecipitating it with acid, in 6N-hydrochloric acid (4·5 ml.) and 50% hypophosphorous acid (2·5 ml.) under reflux for 30 minutes; on storage for 12 hours crystals separated. These were washed with dilute hypophosphorous acid and absolute alcohol and dried in a vacuum at room temperature [Found: Ge, 42·1; Cl, 20·9; P, 18·4. $Ge(H_2PO_2)_2,GeCl_2$ requires Ge, 41·95; Cl, 20·5; P, 17·9%]. If too concentrated solutions were used, or if the solution was cooled too quickly, an amorphous precipitate of $Ge(H_2PO_2)_2,GeCl_2$ was obtained.

Double Salt, $3Ge(H_2PO_2)_2,GeBr_2$.—This *salt* (m. p. 129°) was prepared similarly from activated germanium dioxide (0·5 g.), 35% hydrobromic acid (4 ml.), and 50% hypophosphorous acid (2 ml.); on slow cooling crystals separated. A better method, which more readily gave a crystalline precipitate, was to reduce a solution of activated germanium dioxide (0·4 g.) in 35% hypophosphorous acid (3·5 ml.) by heating it at 100° for 40 minutes; 46% hydrobromic acid (0·5 ml.) was then added and on cooling for 12 hours crystals were obtained [Found: Ge, 35·2; Br, 19·0; P, 22·3. $3Ge(H_2PO_2)_2,GeBr_2$ requires Ge, 34·6; Br, 19·0; P, 22·1%]. In the above two preparations an inert atmosphere was maintained although these compounds were sufficiently resistant to oxidation to permit their isolation in the presence of gaseous oxygen.

The author thanks Mr. H. Terrey, B.Sc., under whose direction part of this work was undertaken, for his interest and advice, and Imperial Chemical Industries Limited for a grant which partly defrayed the cost.

University College, Gower Street, London, W.C.1.
Battersea Polytechnic, London S.W.11.

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308. *Nucleophilic Displacement of Fluorine from Organic Compounds. Part II.* Kinetics of the Reactions of Alkyl Fluorides with Ethanolic Sodium Ethoxide.*

By N. B. Chapman and J. L. Levy.

With ethanolic sodium ethoxide primary alkyl fluorides undergo almost exclusively substitution, at rates 10^3—10^4 times smaller than those for the corresponding bromides. The reactions of primary fluorides and bromides differ little in energy of activation, the lower rates with the fluorides being due to low values of A. Both these facts are probably connected with a highly solvated transition state for fluorides. Secondary and tertiary fluorides undergo a predominating elimination at rates 10^5—10^6 times smaller than those for the corresponding bromides. The reactions of tertiary fluorides are characterised by increased energy of activation and diminished values of A relatively to bromides. The influence of structure of the alkyl group on the rates of substitution and elimination is roughly parallel for bromides and fluorides, but for fluorides the proportion of elimination decreases with increasing temperature, whereas the opposite is true for bromides.

In Part I * of this series one of us discussed the ready displacement of fluorine from 1-fluoro-2 : 4-dinitrobenzene by weakly nucleophilic reagents. We now turn to alkyl fluorides where much more vigorous conditions are necessary to displace the fluorine. The reactions with nucleophilic reagents of alkyl halides other than fluorides have been extensively investigated during the last two decades : our object is to provide comparable results for alkyl fluorides and to elucidate the causes of their inertness.

The remarkable resistance of alkyl fluorides to alkaline hydrolysis has been known for some years (Swarts, *Bull. Acad. roy. Belg.*, 1921, **7**, 438 ; Bockemüller, *Annalen*, 1933, **506**, 25). Even secondary and tertiary alkyl fluorides, although often thermally unstable, display a relatively high stability towards alkali in solution. Recently Hoffmann (*J. Org. Chem.*, 1950, **15**, 429) has studied quantitatively the reactions of ω-bromo-ω-fluoro- and ωω'-difluoro-alkanes with results confirming the difficulty of displacement of the fluorine.

There have been, however, very few kinetic studies. Cooper and Hughes (*J.*, 1937, 1183) briefly record the rate of hydrolysis of *tert.*-butyl fluoride—about 1000 times slower than that of the chloride. McCabe and Warner (*J. Amer. Chem. Soc.*, 1948, **70**, 4031) report the relatively slow bimolecular hydrolysis of fluoroethanol by hydroxyl ions and by water ; and Bernstein and Miller (*J. Amer. Chem. Soc.*, 1948, **70**, 2312, 3600) report the bimolecular reactions of a series of substituted benzyl fluorides with ethanolic sodium ethoxide and with aqueous ethanol. Also the kinetics of the reactions of 2-fluorohexane and *sec.*-amyl fluoride with sodium iodide in acetone have been studied by Bergmann, Polanyi, and Szabo (*Trans. Faraday Soc.*, 1936, **32**, 843). In all these reactions the fluoro-compounds reacted much more slowly than the corresponding chlorides. We now present the results of a systematic investigation of the kinetics of the reactions of primary, secondary, and tertiary alkyl fluorides, mainly fluorobutanes and fluoropentanes, with ethanolic sodium ethoxide. These have been chosen because they can be prepared from accessible starting materials, because, being liquids—lower alkyl fluorides are gases—they can, for the most part, be suitably purified by fractional distillation, and because the reactions of several of the corresponding bromides and chlorides have been carefully studied.

Experimental

Materials.—Alkyl fluorides were prepared (*a*) by the action of an alkyl bromide on potassium fluoride dissolved in ethylene glycol (Hoffman, *J. Org. Chem.*, 1950, **15**, 430) or (*b*) by addition of anhydrous hydrogen fluoride to an olefin (McElvain and Langston, *J. Amer. Chem. Soc.*, 1944, **66**, 1759). Method (*b*) was used for secondary and tertiary fluorides, and method (*a*) mainly

* Part I, *J.*, 1951, 3301.

for primary fluorides. In (*a*) the initial alcohols and bromides, and the final fluorides, were carefully fractionated through a 50-cm. Fenske column, the main fraction having a boiling range of less than 0·2°. Three samples of *n*-amyl alcohol were used: (i) *n*-amyl alcohol (at least 85% pure) from British Drug Houses Ltd., (ii) synthetic *n*-amyl alcohol from Messrs. Boots, and (iii) a sample prepared by the action of formaldehyde on *n*-butylmagnesium bromide. The physical properties of these and other fluorides are assembled in Table 1.

The olefins required for method (*b*) were prepared by dehydration of the corresponding alcohol, except for *cyclo*hexene which was purchased from British Drug Houses Ltd. *tert.*-Amyl alcohol was dehydrated by warming it with dilute sulphuric acid, and *tert.*-butyl and *n*-amyl alcohol were dehydrated by passing the vapour over activated alumina at 200—300°.

*cyclo*Hexyl and *tert.*-amyl fluoride were distilled at reduced pressures to avoid thermal decomposition.

The ethanol used as solvent was dried by Lund and Bjerrum's method (*Ber.*, 1931, **64**, 210) and fractionated. It was shown to contain between 0·04 and 0·07% of water by Karl Fischer

TABLE 1.

Compound	B. p./mm.	B. p. range	n_D^{20}	n_D^{25}
n-Amyl fluoride (i)	64·2°/761	0·2°	1·3590	—
,, (ii)	64·2°/754	0·03	1·3593	1·3569
,, (iii)	64·0°/750	0·00	1·3593	1·3570
n-Butyl fluoride	32·2°/755	0·05	—	—
2-Methyl-*n*-butyl fluoride *	56·2°/577	0·10	1·3570	1·3542
*iso*Amyl fluoride	56·1°/757	0·10	1·3572	1·3547
sec.-Amyl fluoride (i)	56·2°/756	0·15	1·3578	1·3550
,, (ii)	56·3°/738	0·2	1·3588	—
sec.-Butyl fluoride	24·7°/765	0·3	—	—
*cyclo*Hexyl fluoride	43·2°/100	0·2	1·4149	1·4123
tert.-Butyl fluoride	Unobserved	—	1·3320 (1·5° c.)	—
tert.-Amyl fluoride	22·0°/300	0·2	1·3481	—

* $[\alpha]_D$ 0°.

TABLE 2.

n-*Amyl fluoride at* 120·0°. *Initial* NaOEt = 1·017M; *initial* n-$C_5H_{11}F$ = 0·877M. *Concns. are expressed in ml. of* 0·3700N-HCl *per* 4·07 *ml. of reacting solution.*

Time (secs.) × 10^{-4}	0·00	0·80	1·81	2·60	4·47	6·86	10·09	18·36
NaOEt	11·20	10·18	9·29	8·63	7·54	6·55	5·76	4·34
n-$C_5H_{11}F$	9·66	8·64	7·75	7·09	6·00	5·01	4·22	2·80
10^5k	—	1·43	1·32	1·33	1·28	1·25	1·16	1·13

Mean $k = (1·27 \pm 0·08) \times 10^{-5}$. Corr. for solvent expansion, $k = (1·45 \pm 0·09) \times 10^{-5}$.

With initial NaOEt = 0·539M and initial n-$C_5H_{11}F$ = 0·432M, mean $k = (1·26 \pm 0·02) \times 10^{-5}$. Corr. for solvent expansion, $k = (1·44 \pm 0·02) \times 10^{-5}$.

cyclo*Hexyl fluoride at* 139·1°. *Initial* NaOEt = 1·092M; *initial* $C_6H_{11}F$ = 0·889M.

Time (secs.) × 10^{-4}	0·00	10·28	17·81	25·40	34·26	44·16	58·55
NaOEt	12·02	10·45	9·59	8·85	8·20	7·66	6·67
$C_6H_{11}F$	9·89	8·32	7·46	6·72	6·07	5·53	4·54
10^6k	—	1·66	1·63	1·64	1·60	1·55	1·67

Mean $k = (1·63 \pm 0·03) \times 10^{-6}$. Corr. for solvent expansion, $k = (1·95 \pm 0·04) \times 10^{-6}$.

tert.-*Amyl fluoride at* 119·7°. *Initial* NaOEt = 1·000M; *initial* tert.-$C_5H_{11}F$ = 1·149M.

Time (secs.) × 10^{-4}	0·00	5·47	9·27	14·28	22·88	32·57	46·35
NaOEt	12·62	11·86	11·51	10·95	10·08	9·59	8·58
tert.-$C_5H_{11}F$	10·98	10·22	9·87	9·31	8·44	7·95	6·94
10^6k	—	1·22	1·07	1·10	1·14	1·01	1·06

Mean $k = (1·11 \pm 0·06) \times 10^{-6}$. Corr. for solvent expansion, $k = (1·27 \pm 0·06) \times 10^{-6}$.

n-*Butyl fluoride at* 89·8°. *Initial* NaOEt = 1·141M; *initial* Bu^nF = 0·853M. (Concns. in ml. of 0·3710N-HCl per 4·07 ml.)

Time (secs.) × 10^{-4}	0·00	6·62	15·32	24·06	30·98	39·93	50·27	60·07
NaOEt	12·53	11·64	10·73	9·96	9·46	8·97	8·41	8·07
Bu^nF	9·36	8·47	6·56	6·79	6·29	5·80	5·24	4·90
10^6k	—	1·39	1·33	1·32	1·31	1·26	1·25	1·20

Mean $k = (1·29 \pm 0·05) \times 10^{-6}$. Corr. for solvent expansion, $k = (1·41 \pm 0·05) \times 10^{-6}$.

titration. Ethanolic sodium ethoxide was prepared by dissolving clean sodium in ethanol purified as above.

Procedure.—Aliquot portions, usually 4·07 ml., of a standard solution of an alkyl fluoride and sodium ethoxide in anhydrous ethanol were enclosed in "Pyrex" tubes having a minimum vapour space. After being heated in a thermostat for a suitable time, the mixture was added to an excess of standard hydrochloric acid which was back-titrated potentiometrically with standard sodium hydroxide, a quinhydrone electrode and silver–silver chloride half-cell being used. It was shown that the end-point in acid–alkali titrations was not sensibly affected by molar concentrations of sodium fluoride. Olefins were estimated by the extraction method of Hughes and Ingold (*J.*, 1940, 910), but carbon tetrachloride was used as solvent in place of chloroform. Second-order rate coefficients were evaluated by using the equation $k = \frac{1}{(a-b)t} \ln \frac{b}{a} \cdot \frac{a-x}{b-x}$, where a = initial [NaOEt], b = initial [fluoride], x = moles of fluoride consumed, and t = time, rate coefficients being given in l. mole^{-1} sec.$^{-1}$. The mean deviation from the mean is quoted after the mean rate coefficient. Table 2 shows examples, and all the results are collected in Table 3.

TABLE 3.

Compound	Temp.	10^4k	Mean deviation, %	Olefin, %
n-Amyl fluoride (i)	119·0°	12·9	7·1	—
,,	119·0	13·5	7·1	—
,,	89·8	1·25	4·3	—
,,	89·8	1·18	6·3	—
n-Amyl fluoride (ii)	138·6	59·5	6·4	—
,,	120·9	16·0	6·5	—
,,	120·0	14·5	6·2	1·3
,,	89·8	1·44	3·1	0·5
,,	89·8	1·39	3·2	—
,,	79·8	0·563	2·4	2·1
n-Amyl fluoride (iii)	120·2	14·8	3·6	—
,,	89·8	1·40	2·4	—
,,	79·8	0·578	3·4	—
n-Butyl fluoride ...	120·8	15·1	3·8	—
,, ...	120·8	15·5	3·4	—
,, ...	104·9	4·54	4·4	—
,, ...	89·8	1·43	3·4	—
,, ...	89·8	1·41	3·8	—
*iso*Amyl fluoride ...	119·0	4·3	15	12
,, ...	119·0	5·3	5·3	—
,, ...	119·0	5·0	5·1	—
,, ...	89·8	0·53	19	—
,, ...	89·8	0·52	4·2	—
,, ...	138·6	—	—	6·0
2-Methyl-*n*-butyl fluoride	120·8°	3·3	13	10
,, ,,	120·8	3·7	14	—
,, ,,	100·0	0·89	15	—
,, ,,	89·8	0·33	23	—
,, ,,	138·6	—	—	7·5
*cyclo*Hexyl fluoride ...	161·7	10·5	5·2	80·3
,, ...	160·8	10·0	8·3	75
,, ...	147·8	3·96	5·0	—
,, ...	139·1	1·95	2·1	90
,, ...	138·3	1·92	2·2	94
sec.-Amyl fluoride (i)	139·1	3·9	12	83
sec.-Amyl fluoride (ii)	161·7	19	12	60
,, ,,	138·4	3·4	7·6	82
sec.-Butyl fluoride ...	120·0	0·94	4·4	71
tert.-Butyl fluoride ...	118·5	1·46	6·9	95
,, ...	138·5	6·9	7·8	96
tert.-Amyl fluoride ...	119·7	1·27	5·2	95
,, ...	139·7	5·8	4·9	89

DISCUSSION

The low specific rates of these reactions necessitate the use of relatively high temperatures (up to 160°) and approximately molar concentrations if the reactions are to occur with reasonable speeds. Heating molar ethanolic sodium ethoxide in "Pyrex" glass tubes at 140° for six days caused only negligible loss of alkali, possibly by very slight attack on the glass, so no difficulties arise on this account. In aqueous ethanol, however, the loss of alkali is considerable; consequently we have not been able to study these reactions in aqueous ethanolic media, although it was desirable to do so. Certain other complications, however, do arise, particularly the deviation from any integral-order rate law, especially noticeable at higher temperatures. Second-order rate coefficients tend to decrease as a reaction proceeds, more markedly at high temperatures. Nevertheless, except for 2-methyl-*n*-butyl and *iso*- and *sec.*-amyl fluoride, the mean deviation of observed values of second-order velocity coefficients at all but the highest temperatures does not often exceed 5%. We have found no evidence even with tertiary fluorides of first-order reactions under the conditions we employ. Consequently we believe the reactions studied to pursue the bimolecular mechanism found most typically with other primary halides in

reactions with ethanolic sodium ethoxide. At the higher temperatures it is possible that a significant proportion of the fluoride may be in the vapour phase. However, use of bulbs in which the " free " space was restricted to ~2 c.c. probably limits the amount of fluoride in the vapour phase to 3%, so no correction for this has been attempted. With *n*-amyl fluoride we took special steps to ensure that impurities were not vitiating the results: the fluoride was prepared from *n*-amyl alcohol from three sources, including a carefully purified synthetic specimen (cf. p. 1674). Two of the samples of fluoride gave virtually the same results, the third (from commercial *n*-amyl alcohol) showed slight differences, probably due to small amounts of impurities. With the other amyl fluorides, save *tert.*-amyl fluoride, physical properties lie so close together that it is difficult to be certain of the purity of a given specimen; so the results with *iso*amyl and 2-methyl-*n*-butyl fluoride are of qualitative value only. With *sec.*-amyl fluoride prepared by two independent methods, physical properties and rates of reaction were almost the same (Tables 1 and 3).

Table 4 summarises our results for the overall (combined substitution and elimination)

TABLE 4.

(k and A in l. mol.$^{-1}$ sec.$^{-1}$. E is accurate to $\pm$900 cals., A to $\pm$0·5 unit.)

		Bromides		Fluorides	
Alkyl	Temp.	k [a]	k [b]	E (kcal.)	log A
n-Amyl	55°	3·92 × 10^{-4}	8 × 10^{-8}	22·1	7·4
n-Butyl	55	4·39 × 10^{-4}	6 × 10^{-8}	21·8	7·3
sec.-Amyl	25	3·43 × 10^{-6}	1 × 10^{-11}	~27	~8·7
tert.-Amyl	25	5·90 × 10^{-6}	6 × 10^{-11}	24·4	7·7
tert.-Butyl	25	3·00 × 10^{-5}	6 × 10^{-11}	24·8	8·0
*iso*Amyl	55	—	2 × 10^{-8}	~22	~6·9
2-Methyl-*n*-butyl	55	—	2 × 10^{-8}	~21	~6·0
*cyclo*Hexyl	55	—	4 × 10^{-10}	26·4	8·2

[a] Except for Bu^{t}Br, taken from Hughes, Ingold, *et al.*, *J.*, 1948, 2038 *et seq.* [b] Extrapolated from values at higher temps. Only one significant figure is given because of the considerable extrapolation. See Table 3 for observed values.

TABLE 5. *Elimination and substitution in alkyl fluorides and bromides.*

(k_S is the velocity coefficient for bimolecular substitution, k_E for bimolecular elimination, in l. mole^{-1} sec.$^{-1}$).

	Bromides at 55·0° [a]		Fluorides at 120·0°	
Alkyl	$10^5 k_S$	$10^5 k_E$	$10^5 k_S$	$10^5 k_E$
n-Butyl	39·6	4·3	—	—
n-Amyl	35·7	3·5	1·41	0·02
*iso*Butyl	5·8	8·5	—	—
*iso*Amyl	—	—	0·49	0·05
2-Methyl-*n*-butyl	—	—	0·30	0·04
sec.-Butyl	2·3	10·3 [b]	0·027	0·067 [b]
sec.-Amyl	2·0	8·3 [b]	0·014	0·060 [b]
tert.-Butyl	3	90 [b]	0·007	0·139
tert.-Amyl	6	177 [b]	0·006	0·121
*cyclo*Hexyl	—	—	0·005	0·038 [b]

[a] Hughes, Ingold, *et al.*, *J.*, 1948, 2038 *et seq.* [b] Extrapolated from results at other temps.

reactions of alkyl fluorides with ethanolic sodium ethoxide: available overall velocity coefficients for the reactions of corresponding alkyl bromides are included. For the primary halides, where the predominating process at 55° is substitution (Table 5), the bromides react ~5000—7000 times faster than the fluorides. The most comparable value of the energy of activation is for substitution with *iso*butyl bromide, *viz.*, 23 kcal. (Hughes and Dostrovsky, *J.*, 1946, 173), and differs little from those of the primary fluorides, so that the large fall in rate of substitution is due to a fall in log A from 11·0 to ~7·4. This suggests the conclusion that, as with 1-fluoro-2 : 4-dinitrobenzene (see Part I), in comparison with the corresponding bromides, solvation of the incipient fluoride ion in the transition state enables the reaction to pursue a course much more economical of activation energy than would otherwise be possible in view of the probable large dissociation energy of the carbon–fluorine bond. For tertiary halides the predominating reaction is elimination and the most comparable Arrhenius parameters are those for the elimination reaction of

tert.-butyl bromide (Hughes, Ingold, *et al.*, *J.*, 1948, 2050). Here again for the fluorides we observe a value of log A lower by two units than for the bromide, but the energy of activation is increased from ~20 to ~24 kcal., so that the rate ratio is even larger, *viz.*, 10^5—10^6. Solvation of the incipient fluoride ion is again probably a major factor, but is apparently insufficient to reduce the energy of activation with the tertiary fluorides to a value as low as that for the bromides.

The influence of the structure of the alkyl group on the rates of substitution and elimination is roughly parallel for alkyl fluorides and bromides (Table 5). The features common to bromides and fluorides are those already well-known (Hughes, Ingold, *et al.*, *J.*, 1948, 2093), but there is one exception. With fluorides the rate of elimination is much less sensitive to alkyl structure than is the rate of substitution (Table 5). This difference in sensitivity does not seem so marked with bromides, but the rates of bimolecular substitution for tertiary bromides are only available as upper limits, so we pursue this point no further. With secondary fluorides, the predominating process is elimination, but the overall rates are less than for either tertiary or primary fluorides, so that we find for elimination the rate sequence primary < secondary < tertiary, and *vice versa* for substitution. Also, although our olefin determinations are subject to considerable uncertainty, Table 3 shows that the olefin proportions tend to decrease with increasing temperature, in notable contrast with the bromides where there is an increase.

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309. *Nucleophilic Displacement of Fluorine from Organic Compounds. Part III.* Acid-catalysed Solvolysis of Alkyl Fluorides in Aqueous Ethanol.*

By N. B. CHAPMAN and J. L. LEVY.

Graphs illustrating the course of reaction in the acid-catalysed solvolysis in 80% aqueous ethanol of primary, secondary, and tertiary alkyl fluorides are presented. Solvolyses of tertiary fluorides are of the first order with respect to fluoride. The reaction involves attack by a solvated proton on the fluorine, and a process very similar to the unimolecular solvolysis of alkyl chlorides and bromides. Apparent zeroth-order reactions are sometimes observed, but these are thought to be fortuitous. The solvolyses of secondary and primary alkyl fluorides are autocatalytic when the initial acid concentration is low, by virtue of the generated hydrofluoric acid. The variation with structure of mean rate of reaction is far greater in solvolyses of alkyl fluorides than in reactions with ethanolic sodium ethoxide. Alkyl fluorides are often much more stable to heat in ethanolic solution, even in the presence of ethoxide ions, than in the liquid or gaseous phase.

SOLVOLYSIS of alkyl and arylalkyl chlorides and bromides has been very widely investigated (numerous papers by Hughes and Ingold and their co-workers, *J.*, 1940, 1946, 1948), but the solvolysis of alkyl fluorides has received hardly any attention. Cooper and Hughes (*J.*, 1937, 1183) briefly discussed the solvolysis of *tert.*-butyl fluoride, and Bernstein and Miller (*J. Amer. Chem. Soc.*, 1948, **70**, 3600) recorded the percentage reaction after a given time when substituted benzyl fluorides are heated under reflux with 70% aqueous ethanol containing various concentrations of hydrogen chloride. The rate of reaction depends on the initial concentration of hydrochloric acid, in contrast with Olivier and Berger's observations (*Rec. Trav. chim.*, 1922, **41**, 637) with benzyl, *n*-butyl, and *iso*butyl chloride, the solvolyses of which were unaffected by added hydrochloric acid. The present communication records studies of the overall reaction in the solvolysis of a series of alkyl monofluorides, with and without added hydrochloric acid. For reasons to be discussed later, the results are presented graphically in Figs. 2—6, and no attempt has

* Part II, preceding paper.

been made to attribute velocity coefficients to the various reactions, except in a few special cases, and then only approximately.

Experimental

Materials.—Alkyl fluorides were prepared, and ethanol was purified, as recorded in Part II (*loc. cit.*).

Procedure.—Thermostats were as described previously. Reactions were followed by titration with aqueous sodium hydroxide (phenolphthalein) of the total acidity produced when aqueous-ethanolic alkyl fluorides, with or without added hydrochloric acid, were heated in a thermostat for definite times. The samples were enclosed in sealed "Pyrex" bulbs with minimum "free" space: bulbs of the same glass and nearly the same dimensions were used throughout.

Table 1. *Reaction of* tert.*-amyl fluoride with* 80% *aq.* EtOH *at* 79·8° *in the presence of* 0·0148N*-hydrochloric acid.* Initial $[C_5H_{11}F] = 0·1949$M (cf. Fig. 2, *B*).

Time (sec.) × 10^{-3}	2·70	5·82	9·00	12·84	17·46	21·72	25·80
Decompn. (uncorr.), %	7·5	15·4	22·9	29·4	40·1	48·9	51·9
Decompn. (corr.), %	8·8	18·1	26·9	34·6	47·2	57·5	61·0
10^5k (sec.$^{-1}$) (uncorr.)	2·92	2·88	2·90	2·72	2·95	3·09	2·83
10^5k (sec.$^{-1}$) (corr.)	3·40	3·42	3·47	3·30	3·65	3·94	3·64

Mean k, uncorr. = 2·90 × 10^{-5}; mean deviation = 0·09.
Mean k, corr. = 3·54 × 10^{-5}; mean deviation = 0·17.

Results.—Our observations, for the most part, do not permit us to determine velocity coefficients for the reactions, so a selection of the results is presented graphically in Figs. 2—6.

Fig. 1.

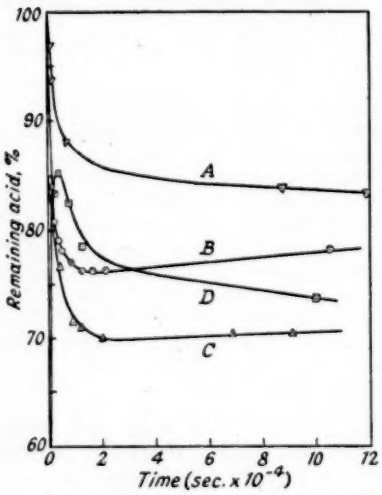

Fig. 2.

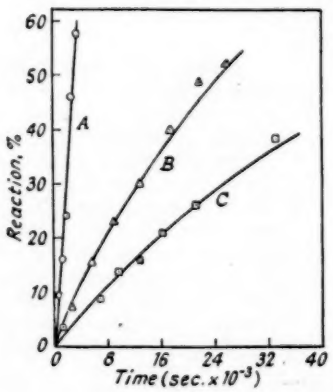

Fig. 1. *Reaction of* HF *in* 80% *aqueous ethanol with "Pyrex" glass.*

	Temp.	*Initial* [HF]	*Initial* [HCl]
A	80°	0·576M	—
B	139·1	1·150M	—
C	138·4	0·457M	0·0742M
D	89·8	*Illustrative example in* Bu^{t}F *solvolysis, zero of time being taken as "infinite" time in the solvolytic reaction.*	

Fig. 2. *Reaction of* tert.*-amyl fluoride in* 80% *aqueous ethanol at* 79·8°.

	A	*B*	*C*
Initial [tert.-$C_5H_{11}F$] (M)	0·894	0·1949	0·1123
Initial [HCl] (M)	0·0742	0·0148	0·0074

In Table 1 results are given in detail for one of the reactions approximating to first-order behaviour and of special importance (cf. p. 1681). These results are given both with and without a correction for loss of hydrofluoric acid by reaction with glass. The correction has been made by assuming that the hydrofluoric acid formed is always in equilibrium with the glass (cf. below), and utilising the appropriate curve from Fig. 1.

The loss of acidity due to reaction of hydrofluoric acid with glass is displayed in Fig. 1, and that due to interaction of ethanol and hydrochloric acid is shown Table 2.

TABLE 2.

Temp.	80°	120°	140°	160°
HCl at equilibrium, %	95	~70—80	27	16
Time reqd. for equilibrn. (sec.)	$\sim 3 \times 10^5$	—	$\sim 3 \times 10^4$	—

Occasionally the solvolyses were conducted in the presence of powdered glass (~3 g. per bulb) without significant influence on the results.

DISCUSSION

Preliminary experiments, summarised in Fig. 1, showed that, when aqueous ethanolic hydrofluoric acid is heated in sealed bulbs at ~80° and ~140°, equilibrium, at which some 70—85% of the initial titratable acidity remains (depending on the temperature), is established within ~330 minutes, *i.e.*, the mean rate of attainment of this equilibrium is large relatively to those of most of the reactions studied. In any given solvolysis the apparent rate of the reaction, as illustrated in Figs. 2—6, depends on the true rate of

FIG. 3.

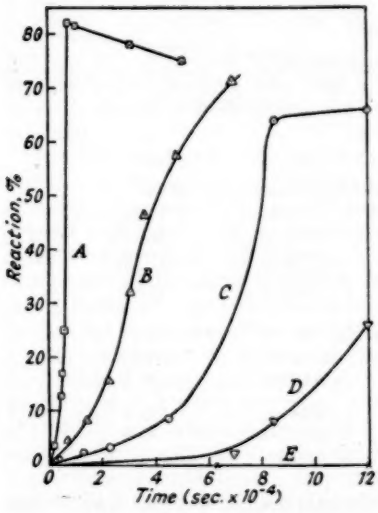

FIG. 4.

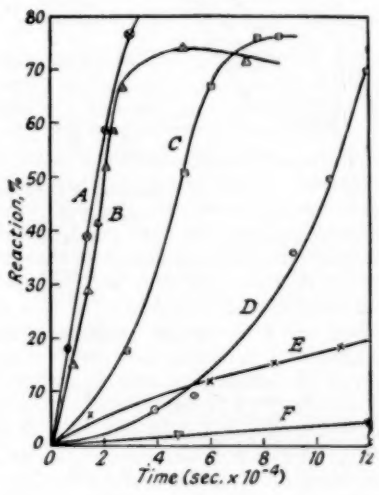

FIG. 3. *Reactions of* tert.*-amyl fluoride in aqueous ethanol at* 79·8°.

	Initial [tert.-$C_5H_{11}F$]	*Solvent*	*Initial* [HCl]
A	0·863M	80% EtOH	0·0074M
B	0·795M	"	*Nil*
C	0·1488M	70% EtOH	*Nil* + 0·126M-NaCl
D	0·1650M	"	*Nil*
E	0·843M	100% EtOH	"

FIG. 4. *Reactions of* cyclo*hexyl fluoride in* 80% *aqueous ethanol at* 138·4°.

	Initial [$C_6H_{11}F$]	*Initial* [*acid*]		*Initial* [$C_6H_{11}F$]	*Initial* [*acid*]
A	0·731M	0·0814N-H_2SO_4	*D*	0·684M	0·0074M-HCl
B	0·983M	0·0742M-HCl	*E*	0·1834M	"
C	0·698M	0·0296M-HCl	*F*	0·773M	0·094N-H_3PO_4

production of acid in solvolysis and the rate of loss of acid by reaction with the glass. Therefore, apart from the most rapid solvolyses, the form of the various curves in Figs. 2—6 will not be significantly affected relatively to each other because of the action on glass of the hydrofluoric acid formed. There is also a loss of acidity due to interaction of ethanol and added hydrochloric acid (cf. Table 2). This has been allowed for by using the acid value of the first sample titrated in any experiment as zero, or by making appropriate corrections from blank experiments. Also this loss of acid is always relatively small, since the initial concentration of hydrochloric acid is $>10\%$ of that of the hydrofluoric acid produced in the reaction. In specifying the concentration of added hydrochloric

FIG. 5.

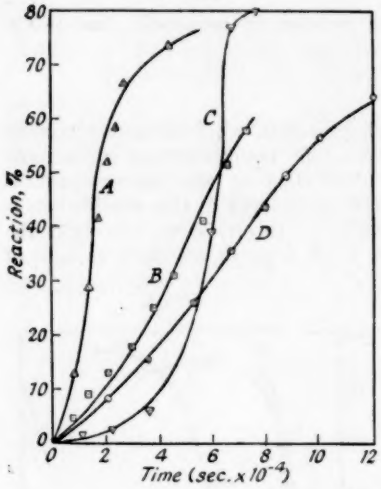

FIG. 6.

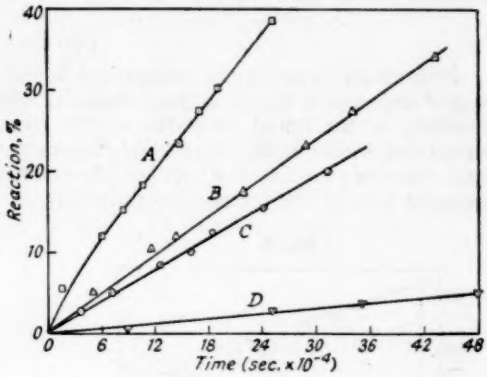

FIG. 5. *Reactions of* cyclo*hexyl fluoride: solvent and temperature effects.*

	Initial [$C_6H_{11}F$]	*Initial* [HCl]	*Solvent*	*Temp.*
A	0·983M	0·0742M	80% EtOH	138·4°
B	0·910M	,,	70% EtOH	119·5
C	0·867M	0·1236M	100% EtOH	139·7
D	0·904M	0·0742M	80% EtOH	119·8

FIG. 6. *Reactions of alkyl fluorides with* 80% *aqueous ethanol.*

	Initial [AlkF]	*Initial* [HCl]	*Temp.*
A. cyclo*Hexyl*	0·1534M	0·0074M	138·4°
B. sec.-*Amyl*	0·1680M	,,	,,
C. n-*Amyl* *	0·420M	0·037M	159·5
D. 2-*Methyl*-n-*butyl*	0·172M	0·0074M	138·4

* *In* 70% EtOH.

acid, no account has been taken of interaction with the ethanol. The total likely errors, being small and all in the same sense, are not such as to obscure the considerable differences between the various curves. Consequently, while we regard our results as relatively valid among themselves, the calculation of rate coefficients is not generally warranted. Moreover, we have made no correction for the loss of hydrofluoric acid by reaction with glass in plotting the curves which summarise our results, because a correction is of importance only where reactions approximate to a first-order law. Table 1 shows that making the maximum correction does not cause serious divergence from first-order behaviour (mean deviations of ~3% and ~5% for uncorrected and corrected values of k).

The variation of mean rate of reaction with structure is far greater in solvolysis of alkyl fluorides than in overall reactions with ethanolic sodium ethoxide. Thus with *n*-amyl fluoride, even at 160° in the presence of 0·0741N-hydrochloric acid, only ~5%

reaction has occurred after $4{\cdot}8 \times 10^5$ seconds, whereas with *tert.*-amyl fluoride and the same hydrochloric acid concentration at 80°, 5% reaction has occurred after ~400 seconds. As an increase in temperature of 20° increases the rate roughly four times, the mean rate ratio is of the order of 10^5—10^6, compared with ~40 for the overall reaction with ethanolic sodium ethoxide.

From the standpoint of kinetic form, the solvolyses of alkyl fluorides are divisible into three main classes: (*a*) approximately first-order reactions, (*b*) apparently zeroth-order reactions, (*c*) autocatalytic reactions. The first and last are of considerable theoretical significance; the second class is probably fortuitous in origin. The first-order reactions constitute the key to the mechanism.

The reactions of *tert.*-butyl and *tert.*-amyl fluorides with 80% ethanol containing hydrochloric acid (0·007—0·07N) show increasing acidity obeying approximately a first-order law (Figs. 2 and 3 and Table 1)—first order in alkyl fluoride—and the velocity coefficients are, within experimental error, directly proportional to the initial concentration of hydrochloric acid (Table 3).

It is improbable that there is any consumption of acid in the reactions, apart from the hydrofluoric acid destroyed by the glass, since the corrected final acid concentrations approximately correspond stoicheiometrically to the initial alkyl fluoride and added hydrochloric acid. Moreover, if the hydrochloric acid is replaced by sodium chloride the reaction assumes a quite distinct form (Fig. 3). Hence we conclude that the rate-determining step involves the alkyl fluoride and the hydrogen ion, which is, however, not consumed in the reaction.

TABLE 3. *Reactions of* tert.*-butyl and* tert.*-amyl fluoride with* 80% *ethanol at* 79·8° *with added hydrochloric acid.*

Added HCl	Initial Bu^tF	10^5k_1	10^5k/[HCl]	Initial *tert.*-$C_5H_{11}F$	10^5k_1	10^5k_1/[HCl]
0·00742M	0·192M	1·1	1·5	0·112M	1·4	1·9
0·0148M	0·180M	1·9	1·3	0·195M	2·9	1·9
0·0742M	0·811M	12	1·5	0·894M	18	2·4

It seems most likely that we are dealing with acid-catalysed solvolysis in these reactions. The kinetic results do not distinguish between unimolecular and bimolecular solvolysis, since the latter reactions become pseudo-unimolecular. However, the facts that solvolysis is most rapid, and only approximates closely to a first-order law, for tertiary fluorides make it very probable that the mechanism of this acid-catalysed solvolysis is fundamentally similar to that of unimolecular solvolysis of alkyl bromides and chlorides. It is clear that the hydrofluoric acid produced in the solvolysis has very little effect on the observed rate for tertiary fluorides. Two factors probably account for this: (*a*) much of the hydrofluoric acid is converted, by reaction with the glass, into fluorosilicic and fluoroboric acid, with a consequent reduction in the concentration of free acid; and (*b*) hydrofluoric acid is a weak acid (pK_a ~5 for water at 25°). Similar behviour is shown by phosphoric acid, also weak ($pK_a = 2{\cdot}1$ for water at 25°) (cf. Fig. 4). Thus the first-order reaction persists as the reaction proceeds because the rate of the reaction due to hydrofluoric acid is insignificant compared to that due to hydrochloric acid. With relatively high initial fluoride concentrations the hydrofluoric acid becomes significant, and the reactions assume apparent zeroth-order character, even with tertiary halides. It is noteworthy in this connection that Swain, Esteve, jnr., and Jones (*J. Amer. Chem. Soc.*, 1949, **71**, 965) found that the solvolysis of triphenylmethyl fluoride in aqueous methanol and in methanol–acetone was of the first order and unaffected by variation in pH. They worked with a fluoride concentration of 0·001M.

The apparent obedience to a zeroth-order law in the solvolysis of primary fluorides and of secondary fluorides in the presence of hydrochloric acid (Figs. 2, 4, and 6) we regard as fortuitous and arising from a combination of a first-order reaction and significant autocatalysis by the hydrofluoric acid formed. We do not think it conceivable that the rate-determining process can be localised in such a way as to exclude the fluoride molecule in view of the strength of the bond broken and the rapidity of proton transfers.

Autocatalytic reactions are observed in solvolysis in initially neutral solutions or when the ratio of the initial concentration of alkyl fluoride to that of hydrochloric acid exceeds 100 (Figs. 3, 4, and 5). In either case the rate increases with increasing concentration of hydrofluoric acid formed: in the former it is the only acid present, in the latter the hydrochloric acid, being in relatively low concentration, no longer dominates the situation as in previous examples (p. 1681). The solvolyses of secondary alkyl fluorides are either apparently of zeroth order or autocatalytic. At relatively low initial concentrations of hydrochloric acid, the reactions are autocatalytic: at higher concentrations of zeroth order, *i.e.*, probably of first order with superimposed autocatalysis.

The stability of alkyl fluorides to solvolysis in initially neutral anhydrous ethanol is very considerable: thus no detectable reaction occurs when M-*cyclo*hexyl fluoride in ethanol is heated at 140° for 200 hours. Even with M-ethanolic *tert.*-amyl fluoride at 120° no reaction is observable after 4 hours, although after 22 hours 85% reaction has occurred. Pure alkyl fluorides, however, especially *tert.*-butyl and *tert.*-amyl fluoride, are thermally unstable at their boiling points.

The ultimate cause of the acid catalysis in these solvolyses is the great affinity of fluorine for protons, even when solvated (cf. Bernstein and Miller, *loc. cit.*). This behaviour is unique among alkyl halides, but finds an analogy in the solvolyses of other alkyl halides "catalysed" by mercuric and silver salts, where the metallic ions have powerful affinity for the halogen. In contrast with reactions in alkaline media, the driving force of these reactions is an attack on halogen by an electrophilic reagent. However, the overall process may be regarded as a nucleophilic substitution, since the substituting agents are weakly nucleophilic, *viz.*, water and ethanol. The most likely mechanism for these reactions is:

$$RF + H_3O^+ \longrightarrow \underset{H}{\overset{H}{\diagdown}}\!\!>O^+\!\!-\!\!H\cdots F \ldots . R \longrightarrow R^+ + HF + H_2O \text{ (slow)} \quad (1)$$

Transition state

$$R^+ + 2H_2O \longrightarrow ROH + H_3O^+ \text{ (rapid)} \quad (2)$$

The hydrogen fluoride formed will, of course, be partly dissociated. Variants may be suggested, especially one involving rapid and reversible complex-formation between the fluoride and a solvated proton. However, we have at present no experimental evidence to distinguish these mechanisms, so we confine ourselves to the above. Again, as we have no relevant experimental evidence, we have not considered Swain's "push-pull" mechanism (*J. Amer. Chem. Soc.*, 1948, **70**, 1119).

It is clear from this and the preceding paper that the displacement of fluorine from alkyl fluorides is dominated by three characteristic features of fluorine: ability to form hydrogen bonds, ability to form very strong bonds with carbon, and a high degree of solvation of the incipient fluoride ion.

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UNIVERSITY COLLEGE, SOUTHAMPTON. [*Received, December 6th*, 1951.]

310. *Triterpenoids. Part VI.* Some Observations on the Constitution of Zeorin.*

By D. H. R. Barton and T. Bruun.

The saturated triterpenoid diol, zeorin, $C_{30}H_{52}O_2$, isolated from *Nephroma arcticum* L., has been fully characterised. Dehydration of the acetate afforded zeorinin acetate or *iso*zeorinin acetate according to the reagent used. The last ester contains an exocyclic methylene group or its equivalent. Hydrogenation of *iso*zeorin acetate, or hydrogenolysis of zeorin acetate, gave deoxyzeorin acetate. The carbonyl group of deoxyzeorinone and of zeorininone is very hindered; on the basis of infra-red evidence it is contained in a six-membered ring.

Dehydration of deoxyzeorin by toluene-*p*-sulphonyl chloride in pyridine, or pyrolysis of deoxyzeorin benzoate, afforded mixtures of hydrocarbons, converted by hydrogenation and further treatment into the saturated zeorinane. The latter is not identical with any known triterpenoid hydrocarbon.

The classical work of Zopf (*Annalen*, 1909, **364**, 273, and earlier papers) and of Hesse (*J. pr. Chem.*, 1906, **73**, 113) on the constituents of lichens led to the recognition of zeorin as a frequent component of these primitive organisms. For many years the chemistry of zeorin received little attention, until Asahina and Akagi (*Ber.*, 1938, **71**, 980) and Asahina and Yosioka (*ibid.*, 1940, **73**, 742) demonstrated that it was a pentacyclic secondary-tertiary diol, $C_{30}H_{52}O_2$, of the triterpenoid series. Through the kindness of Professor and Mrs. N. A. Sörensen (Trondheim, Norway) in collecting and making available to us a quantity of the lichen *Nephroma arcticum* L., it became possible for us to undertake a further study of zeorin.

Zeorin and a number of its simple derivatives do not exhibit sharp melting points. Our attention was first directed to a verification of the homogeneity of these compounds. This was established by thorough chromatographic fractionation of the acetate and of the benzoate. Oxidation of zeorin by chromic acid afforded zeorinone. This ketone showed infra-red carbonyl maxima at 5·86 μ (in carbon disulphide) and at 5·87 μ (in chloroform), values which are indicative (cf. R. Norman Jones *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 2024) of a keto-group in a six-membered ring. Zeorinone was resistant to the ordinary carbonyl characterising reagents.

Treatment of zeorin acetate with ethanolic hydrochloric acid (Zopf, *Annalen*, 1895, **288**, 50; Asahina and Yosioka, *loc. cit.*) led to dehydration, with formation of the long known zeorinin acetate. The far ultra-violet absorption spectrum of this compound (see Experimental section) indicated that the double bond was of either a tri- or a tetra-substituted type for which reference data are not yet available. Zeorinin acetate was further characterised by hydrolysis to zeorinin and by conversion of the latter into its benzoate. Treatment of zeorinin acetate with perhydrol in acetic acid gave the saturated zeorinin acetate oxide. The benzoate was prepared likewise and, on treatment with hydrochloric–acetic acids, furnished, with loss of water, dehydrozeorinin benzoate. The latter was identified as a conjugated diene by its absorption spectrum ($\lambda_{max.}$ 252 mμ; $\varepsilon_{max.} = 18{,}000$).

Zeorin acetate was dehydrated by phosphorus oxychloride in pyridine to a strongly dextrorotatory isomer of zeorinin acetate, which we designate *iso*zeorinin acetate. This was further characterised by hydrolysis to *iso*zeorinin and by benzoylation of the latter. Similar dehydration of zeorinone gave *iso*zeorininone. On digestion with ethanolic hydrochloric acid *iso*zeorininone was isomerised to zeorininone, also prepared, although in poor yield, by chromic acid oxidation of zeorinin; *iso*zeorinin benzoate was likewise isomerised to zeorinin benzoate. The infra-red spectrum of *iso*zeorinin acetate showed a strong band at 11·28 μ (in carbon disulphide), indicative of an exocyclic (or other) methylene

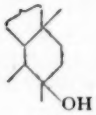
* Part V, *J.*, 1952, 78.

grouping (>C=CH_2), which band is not present in the infra-red spectrum of zeorinin acetate or of zeorinone. We conclude that zeorin contains the grouping >CMe·OH. The "anhydrozeorin acetate," prepared by Asahina and Yosioka (*loc. cit.*) by refluxing zeorin with acetic acid, was probably somewhat impure *iso*zeorinin acetate.

Although Asahina and Yosioka (*loc. cit.*) claimed that zeorinin acetate could be hydrogenated to a "deoxyzeorin acetate" with a palladium catalyst, we have been unable to effect this reduction using a platinum catalyst even under vigorous conditions. *iso*-Zeorinin acetate, on the other hand, was smoothly hydrogenated, to deoxyzeorin acetate, also obtained by hydrogenolysis of zeorin acetate itself. Deoxyzeorin acetate was further characterised by hydrolysis to the alcohol and by conversion into the benzoate. Our series of deoxyzeorin compounds is not identical with the compounds prepared by Asahina and Yosioka (*loc. cit.*). Chromic acid oxidation of deoxyzeorin afforded deoxyzeorininone.

The carbonyl group in zeorinone, zeorininone, and in deoxyzeorinone cannot be situated at the usual $C_{(2)}$ position (as I) in the customary pentacyclic triterpenoid nucleus, because it is resistant to carbonyl reagents and to reduction. Thus Wolff–Kishner and Clemmensen reduction, even under such vigorous conditions as in the preparation of lanostane (Voser, Montavon, Günthard, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 1893; Barton, Bruun, Thomas, and Fawcett, *J.*, 1951, 3154), failed to effect the removal of oxygen from zeorininone. Instead, the vigorous Clemmensen conditions caused partial isomerisation to a further isomer, *neo*zeorininone, m. p. 238—240°, $[\alpha]_D$ −2°, in which the double bond and keto-group had *not* moved into conjugation.

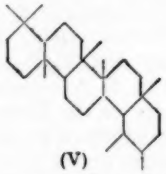
(I)



(II)

(III)

(IV)

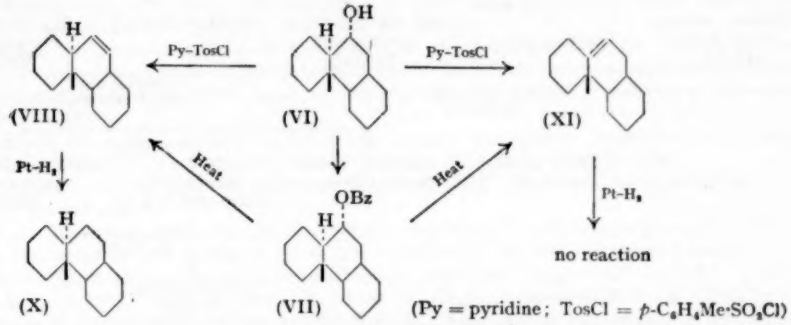

(V)

The ready acylation of zeorin, zeorinin, *iso*zeorinin, and deoxyzeorin, combined with the high degree of steric hindrance of the corresponding carbonyl compounds, must be explained, on the basis of a six-membered ring (see above), by the hydroxyl group of zeorin being equatorial (Barton, *Experientia*, 1950, **6**, 316; Barton and Rosenfelder, *J.*, 1951, 1048). This was confirmed by lithium aluminium hydride reduction of deoxyzeorinone to *epi*deoxyzeorin (see footnote, p. 83, in the paper by Barton and Holness, *J.*, 1952, 78). The latter was smoothly oxidised back to deoxyzeorinone by chromic acid, but it resisted benzoylation under conditions adequate for the benzoylation of deoxyzeorin. Further confirmation came from the reduction of zeorininone to zeorinin by sodium and alcohol (see Barton, *loc. cit.*).

At this stage of the investigation it seemed clear that there might be a parallel between the chemistry of zeorin ($[\alpha]_D$ +54°), *iso*zeorinin ($[\alpha]_D$ +78°), and zeorinin ($[\alpha]_D$ +59°) on the one hand and of ψ-taraxastanediol (Morice and Simpson, *J.*, 1941, 181), taraxasterol ($[\alpha]_D$ +91°) (*e.g.*, Lardelli and Jeger, *Helv. Chim. Acta*, 1948, **31**, 813), and ψ-taraxasterol (*hetero*lupeol) ($[\alpha]_D$ +47°) (Burrows and Simpson, *J.*, 1938, 2042) on the other. Thus the series (II), (III), and (IV) *might* have been adequate partial formulæ for the above-mentioned relations in both series of compounds. It thus became of primary importance to effect the conversion of zeorin into the fundamental saturated hydrocarbon, for this could conceivably have been identical with *hetero*lupane (V). As mentioned above, attempts at the direct removal of the secondary oxygen function (as a carbonyl group) proved abortive. After a number of experiments, zeorinane was eventually obtained in the following two ways. (*a*) Dehydration of deoxyzeorin by toluene-*p*-sulphonyl chloride in boiling pyridine gave a mixture of monoethylenic hydrocarbons, which were hydrogenated by using a platinum catalyst in acetic acid to a mixture of saturated and unsaturated hydrocarbons. After destruction of the unsaturated hydrocarbon by the procedure of Anderson and Nabenhauer (*J. Amer. Chem. Soc.*, 1924, **46**, 1957), the saturated zeorinane remained unattacked. (*b*) Pyrolysis of deoxyzeorin benzoate gave a mixture of mono-

ethylenic hydrocarbons which, on further treatment as under (*a*), also furnished zeorinane. The yield was superior in the former procedure. Zeorinane had m. p. 186·5—187·5°, $[\alpha]_D$ +12°, and closely resembled *hetero*lupane in properties (Jeger, Krüsi, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1048). A reference specimen of the latter hydrocarbon, prepared from taraxasterol by a known route (Lardelli and Jeger, *ibid.*, 1948, **31**, 813) had the same melting point and rotation. However, zeorinane was *not* identical with *hetero*lupane, for there was a pronounced melting point depression on admixture. Zeorinane would appear to be a new fundamental hydrocarbon of the triterpenoid series.

These indirect methods of formation of zeorinane can be plausibly interpreted in terms of the partial formulæ (VI) (for deoxyzeorin), (VII) (for deoxyzeorin benzoate), (VIII), (IX), and (X), the last representing zeorinane. There is analogy for the pyrolysis reaction in the behaviour of 7-benzoyloxy-groups in the cholestane series (Barton and Rosenfelder, *J.*, 1949, 2459).



(Py = pyridine; TosCl = *p*-$C_6H_4Me{\cdot}SO_2Cl$)

In spite of the apparent similarity of reactions and rotations in the zeorin and ψ-taraxastanediol series of compounds (see above) there are at least two major chemical differences. First, ψ-taraxasteryl acetate is readily hydrogenated (Lardelli, Krüsi, Jeger, and Ruzicka, *ibid.*, p. 1159) whereas zeorinin acetate, in our hands at least, is resistant. Secondly, taraxasteryl acetate is readily isomerised by hydrochloric acid in acetic acid to lupenyl-I acetate * whereas, under the *same* conditions, *iso*zeorinin acetate is isomerised to zeorinin acetate, but not further.

The secondary and tertiary hydroxyl groups in zeorin are either not close to each other in the molecule, or else they are separated by fully substituted centres. Thus the double bond and carbonyl group of zeorininone do not move into conjugation on treatment with acid (see above), and the mixture of hydrocarbons obtained by dehydration of zeorinin with toluene-*p*-sulphonyl chloride in pyridine is not isomerised to a conjugated diene by hydrochloric–acetic acids.

Experimental

M. p.s are uncorrected. All rotations were taken in chloroform solution: the values recorded have been approximated to the nearest degree.

Ultra-violet absorption spectra were determined in absolute ethanol solution, with a Unicam Spectrophotometer, Model SP 500. They have not been corrected for instrument error in the far ultra-violet range (cf. Bladon, Henbest, and Woods, *Chem. and Ind.*, 1951, 867).

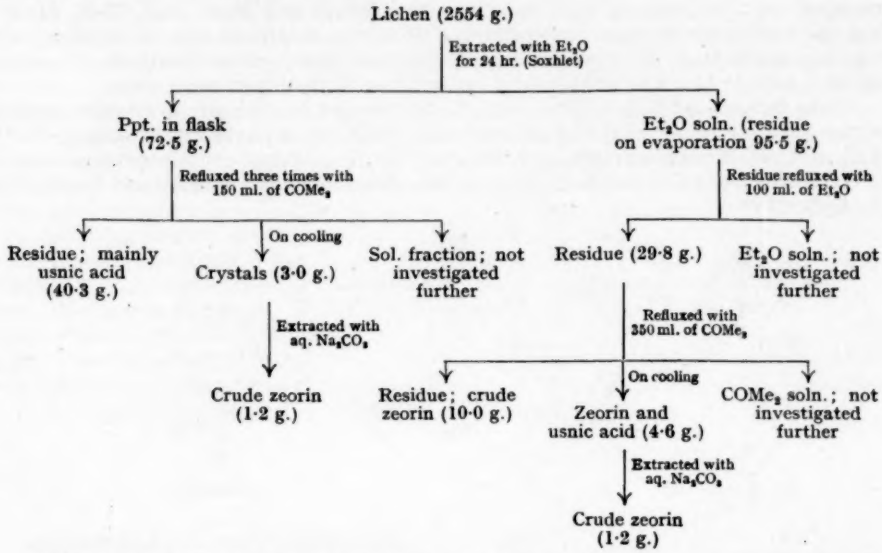
Infra-red absorption spectra were kindly determined by Dr. Hans Heymann (Harvard) and Dr. W. J. Rosenfelder (Harvard), using a Baird Associates (Cambridge, Mass.) recording double-beam instrument.

Alkaline hydrolyses were effected by using several equivalents of potassium hydroxide and refluxing for 30—60 minutes in methanolic or dioxan-methanolic solution depending on the solubility requirements of the ester.

Light petroleum refers throughout to the fraction of b. p. 40—60°.

* This reaction is under investigation by Professor E. R. H. Jones, F.R.S., Dr. T. G. Halsall, and their colleagues at the University of Manchester. It is our understanding that they will present a full report in due course.

Isolation of Zeorin.—Zeorin was obtained by extraction of *Nephroma arcticum* L. with ether according to the flow sheet below. The lichen had been collected by Professor and Mrs. N. A. Sörensen in the Oppdal district of Norway. It was freed from adhering mosses and earth, dried in air, and crushed in a porcelain ball-mill.


Lichen (2554 g.)
Extracted with Et_2O for 24 hr. (Soxhlet)
Ppt. in flask (72·5 g.)
Et_2O soln. (residue on evaporation 95·5 g.)
Refluxed three times with 150 ml. of $COMe_2$
Residue refluxed with 100 ml. of Et_2O
Residue; mainly usnic acid (40·3 g.)
On cooling
Crystals (3·0 g.)
Sol. fraction; not investigated further
Residue (29·8 g.)
Et_2O soln.; not investigated further
Extracted with aq. Na_2CO_3
Refluxed with 350 ml. of $COMe_2$
Crude zeorin (1·2 g.)
Residue; crude zeorin (10·0 g.)
On cooling
Zeorin and usnic acid (4·6 g.)
$COMe_2$ soln.; not investigated further
Extracted with aq. Na_2CO_3
Crude zeorin (1·2 g.)

Purification of Zeorin.—Attempted fractionation of the crude zeorin by crystallisation from alcohol gave fractions with the following constants (in order of increasing solubility) : (i) m. p. 228—245°, $[\alpha]_D$ +48° (*c*, 0·54 in 2-dm. tube), (ii) m. p. 235—247°, $[\alpha]_D$ +53° (*c*, 0·50 in 2-dm. tube), (iii) m. p. 245—253°, $[\alpha]_D$ +54° (*c*, 0·47 in 4-dm. tube), (iv) m. p. 240—248°, $[\alpha]_D$ +55° (*c*, 0·52 in 2-dm. tube). In view of the widely different m. p.s recorded for zeorin in the literature (cf. Abderhalden's " Biochemisches Handlexikon," 1912, Vol. VII (1), p. 56 *et seq.*) and of the wide melting ranges found in our own experiments above, the homogeneity of zeorin was investigated. For this purpose chromatography of zeorin acetate was found convenient.

Crude zeorin (approx. 10 g.) was dissolved in dry pyridine, excess of acetic anhydride added, and the mixture left overnight at room temperature. Working up in the usual way afforded crude zeorin acetate. A small specimen, recrystallised from benzene–light petroleum (b. p. 60—80°), had m. p. 223—230°, $[\alpha]_D$ +75° (*c*, 0·50 in 2-dm. tube). Alkaline hydrolysis gave back a zeorin of m. p. 220—233°, $[\alpha]_D$ +54° (*c*, 0·51 in 2-dm. tube). The bulk of the acetylated crude zeorin was chromatographed over alumina (29 fractions). Elution with 1 : 1 benzene–ether afforded pure zeorin acetate, m. p. 225—230° (unchanged on repeated crystallisation from chloroform–methanol), $[\alpha]_D$ +78° (*c*, 0·53 in 2-dm. tube), +78° (*c*, 0·52 in 2-dm. tube); the resolidified melt had the same m. p. range. It was concluded that, in spite of the wide m. p. range, the homogeneity of the zeorin acetate had been established (Found : C, 79·0; H, 11·05. Calc. for $C_{32}H_{54}O_3$: C, 78·95; H, 11·2%). A subsequent preparation of pure zeorin acetate also showed $[\alpha]_D$ +78° (*c*, 0·54 in 2-dm. tube).

Hydrolysis of zeorin acetate with refluxing 20% methanolic potassium hydroxide gave zeorin which, recrystallised from acetone, had m. p. 223—227°, $[\alpha]_D$ +54° (*c*, 0·50 in 2-dm. tube).

As a further confirmation of the homogeneity, 1 g. of zeorin was converted into the benzoate by being kept overnight in pyridine solution with excess of benzoyl chloride. Working up in the usual way and recrystallisation from benzene–acetone afforded *zeorin benzoate*, m. p. 236—246°, $[\alpha]_D$ +73° (*c*, 0·50 in 2-dm. tube) (Found : C, 80·7; H, 9·95. $C_{37}H_{56}O_3$ requires C, 80·95; H, 10·3%). Chromatography over alumina (30 fractions) demonstrated the homogeneity of the benzoate, $[\alpha]_D$ +75° (*c*, 0·51 in 2-dm. tube), after recrystallisation from acetone.

Zeorinone.—Zeorin (500 mg.) in " AnalaR " acetic acid (40 ml.) was treated with chromium

trioxide (100 mg.) in 0·1 ml. of water and 2 ml. of acetic acid at room temperature, and the solution set aside overnight. The reaction mixture was worked up in the usual way and the product recrystallised from chloroform–methanol, to give *zeorinone*, m. p. 239—245° (decomp.), $[\alpha]_D$ +35° (*c*, 0·57), $\lambda_{max.}$ 300 mμ ($\varepsilon_{max.}$ = 30) (Found: C, 81·2; H, 11·05. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

Zeorinin Acetate.—Zeorin acetate (1·0 g.) was treated with ethanol (132 ml.) and concentrated hydrochloric acid (26 ml.) according to the procedure of Asahina and Yosioka (*Ber.*, 1940, **73**, 742; cf. Zopf, *Annalen*, 1895, **288**, 50). Since the m. p. of the reaction product [m. p. 196—203°, $[\alpha]_D$ +71° (*c*, 0·54) after recrystallisation from chloroform–acetone] was not sharp it was deemed desirable to carry out a chromatographic fractionation (14 fractions) in order to establish its homogeneity. The m. p.s of the fractions ranged from 197—203° to 200—205°, the latter unchanged on repeated recrystallisation, whilst the rotations of the fractions were constant at approx. 70° (see below). It was concluded that, in spite of the wide m. p. range, the homogeneity of the zeorinin acetate had been established. The mean $[\alpha]_D$ based on seven determinations was +70°, $\lambda_{max.}$ 201 mμ ($\varepsilon_{max.}$ = 5500; ε_{215} = 1700) (*c*, 0·004) (Found: C, 81·8; H, 11·45. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%).

Treatment of zeorinin acetate in chloroform at room temperature for 15 minutes with gaseous dry hydrogen chloride, followed by removal of the solvent *in vacuo* and recrystallisation from chloroform–methanol, gave back zeorinin acetate, m. p. and mixed m. p. 200—203°, $[\alpha]_D$ +70° (*c*, 0·59).

Hydrolysis of zeorinin acetate as for zeorin acetate (see above) afforded zeorinin which, recrystallised from acetone–methanol, had m. p. 179—183°, $[\alpha]_D$ +59° (*c*, 0·50).

Asahina and Yosioka (*loc. cit.*) recorded m. p. 181—183°, $[\alpha]_D$ +50° for zeorinin and m. p. 197—200° for the acetate.

Zeorinin Benzoate.—Benzoylation of zeorinin with benzoyl chloride in pyridine overnight at room temperature and working up in the usual way furnished *zeorinin benzoate* which, recrystallised from chloroform–acetone, had m. p. 218—220°, $[\alpha]_D$ +51° (*c*, 0·59), +49° (*c*, 0·53), +50° (*c*, 0·51) (Found: C, 83·4; H, 10·15. $C_{37}H_{54}O_2$ requires C, 83·7; H, 10·25%).

Zeorininone.—*iso*Zeorininone (see below) (150 mg.) was treated with ethanolic hydrochloric acid as for the preparation of zeorinin acetate. Working up in the usual way and recrystallisation from chloroform–methanol furnished zeorininone, m. p. 173—176°. Further treatment in chloroform with hydrogen chloride furnished a more sharply melting preparation, m. p. 177—178°, $[\alpha]_D$ +21° (*c*, 0·50 in 2-dm. tube), $\lambda_{max.}$ 298 (ε = 50) and 200 mμ (ε = 8700; ε_{215} = 2700) (*c*, 0·0042) (Found: C, 84·35, 84·25; H, 11·1, 11·25. Calc. for $C_{30}H_{48}O$: C, 84·85; H, 11·4%). Oxidation of zeorinin by chromic acid at room temperature also afforded zeorininone, $[\alpha]_D$ +23° (*c*, 0·55), $\lambda_{max.}$ 299 mμ (ε = 50), but in very poor yield and only isolatable by careful chromatography. Zeorininone was recovered unchanged on attempted Wolff–Kishner reduction. For zeorininone Asahina and Yosioka (*loc. cit.*) recorded m. p. 184° but no rotation.

Zeorininone (100 mg.) was dissolved in 25 ml. of *n*-propanol and saturated with sodium at the reflux. After working up in the usual way the reaction product was acetylated with acetic anhydride–pyridine at room temperature for 24 hours. After the usual treatment the acetate was recrystallised from chloroform–methanol, to furnish somewhat impure zeorinin acetate, $[\alpha]_D$ +66° (*c*, 1·00), m. p. 190—195° undepressed on admixture with authentic material (see above).

Treatment of zeorininone with hydrochloric and acetic acids, as in the isomerisation of *iso*zeorinin acetate (see above), gave back starting material.

Zeorinin Acetate Oxide.—Zeorinin acetate (200 mg.) in "AnalaR" acetic acid (50 ml.) was heated on the steam-bath for 0·5 hour with addition of perhydrol (1 ml.). After working up in the usual way the reaction product was chromatographed over alumina, elution being with benzene and benzene to which 1% of ether had been added. All fractions melted at 255—258°. They were combined and recrystallised from chloroform–methanol, to give zeorinin acetate oxide, m. p. 255—257°, $[\alpha]_D$ +74° (*c*, 1·06) (Found: C, 78·8; H, 10·85. Calc. for $C_{32}H_{54}O_3$: C, 79·3; H, 10·8%). For this compound Asahina and Yosioka (*loc. cit.*) reported m. p. 255—257° also.

Zeorinin Benzoate Oxide.—Zeorinin benzoate (300 mg.) was treated with acetic acid and perhydrol as above. Recrystallisation of the product from chloroform–methanol gave *zeorinin benzoate oxide*, m. p. 259—260°, $[\alpha]_D$ +67° (*c*, 1·32), +66° (*c*, 1·07) (Found: C, 81·2; H, 9·8. $C_{37}H_{54}O_3$ requires, C, 81·25; H, 9·95%).

Dehydrozeorinin Benzoate.—Zeorinin benzoate oxide (200 mg.) was refluxed for two hours in 10 ml. of "AnalaR" acetic acid and 2 ml. of concentrated hydrochloric acid. After working

up in the usual way the product was filtered through alumina in benzene solution. The eluate was recrystallised from chloroform–methanol, to furnish *dehydrozeorinin benzoate*, m. p. 208—215° $[\alpha]_D$ +41° (*c*, 1·51), +40° (*c*, 1·19), +37° (*c*, 1·02), $\lambda_{max.}$ 235 and 252 mμ (ε = 20,000 and 18,000 respectively) (Found : C, 84·1; H, 10·25. $C_{37}H_{52}O_2$ requires C, 84·05; H, 9·9%). The m. p. was unchanged on repeated fractional crystallisation.

iso*Zeorinin Acetate*.—Zeorin acetate (500 mg.) was treated with phosphorus oxychloride (2 ml.) in pyridine (15 ml.) at room temperature overnight. After working up in the usual way the product was repeatedly recrystallised from chloroform–methanol, to give iso*zeorinin acetate*, m. p. 212—213°, $[\alpha]_D$ +108° (*c*, 0·54), +109° (*c*, 0·52) (Found : C, 81·65; H, 11·05. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Further fractionation did not alter these constants.

Hydrolysis as for zeorin acetate (see above) gave iso*zeorinin* which, recrystallised from acetone, had m. p. 185—202°, $[\alpha]_D$ +78° (*c*, 0·50) (Found : C, 84·3; H, 11·95. $C_{30}H_{50}O$ requires C, 84·45; H, 11·8%). This with benzoyl chloride in pyridine at room temperature overnight gave, after working up in the usual way, iso*zeorinin benzoate*, m. p. 234—236°, $[\alpha]_D$ +100° (*c*, 0·52), from chloroform–methanol (Found : C, 83·05; H, 10·1. $C_{37}H_{54}O_2$ requires C, 83·7; H, 10·25%).

Treatment of *iso*zeorinin benzoate with ethanolic hydrochloric acid as in the preparation of zeorinin acetate (see above) afforded, in almost quantitative yield zeorinin benzoate, $[\alpha]_D$ +51° (*c*, 0·56), m. p. 219—220° undepressed on admixture with the authentic benzoate (see above).

To *iso*zeorinin acetate (400 mg.) in boiling acetic acid (10 ml.), concentrated hydrochloric acid (2 ml.) was added. The refluxing was continued for 30 minutes. Working up in the usual way and recrystallisation from chloroform–methanol gave zeorinin acetate, $[\alpha]_D$ +65° (*c*, 1·77), m. p. 195—198° undepressed on admixture with authentic material (see above). Under the same acid conditions taraxasteryl acetate was smoothly isomerised to lupenyl-I acetate.

iso*Zeorininone*.—Zeorinone (400 mg.) (see above) was treated with phosphorus oxychloride and pyridine as in the preparation of *iso*zeorinin acetate (see above). After working up in the usual way the product was repeatedly recrystallised from chloroform–methanol, to furnish iso*zeorininone*, m. p. 208—212°, $[\alpha]_D$ +31° (*c*, 0·56), +31° (*c*, 0·52), +30° (*c*, 0·50), $\lambda_{max.}$ 299 mμ (ε = 35) (Found : C, 84·5; H, 11·35. $C_{30}H_{48}O$ requires C, 84·85; H, 11·4%).

Deoxyzeorin Acetate.—(a) *Hydrogenation of* iso*zeorinin acetate*.—*iso*Zeorinin acetate (200 mg.) in anhydrous ether (25 ml.) and " AnalaR " acetic acid (75 ml.) was hydrogenated overnight with a platinum catalyst. After working up in the usual way, recrystallisation from chloroform–methanol furnished *deoxyzeorin acetate*, m. p. 202—203°, giving no colour with tetranitromethane (Found : C, 81·0; H, 11·4. $C_{32}H_{54}O_2$ requires C, 81·65; H, 11·55%).

Hydrolysis as for zeorin acetate (see above) gave *deoxyzeorin* which, recrystallised from chloroform–methanol, had m. p. 198—199° (Found : C, 82·6; H, 11·7. $C_{30}H_{52}O,\frac{1}{2}CH_3{\cdot}OH$ requires C, 82·35; H, 12·25%). Deoxyzeorin was further characterised by conversion into the benzoate by benzoyl chloride–pyridine overnight at room temperature. Working up in the usual way gave *deoxyzeorin benzoate*, m. p. 235—236° (from chloroform–methanol), $[\alpha]_D$ +56° (*c*, 0·59) (Found : C, 82·8; H, 10·4. $C_{37}H_{56}O_2$ requires C, 83·4; H, 10·6%).

(b) *Hydrogenation of zeorin acetate*. Zeorin acetate (1·02 g.) in anhydrous ether (50 ml.) and " AnalaR " acetic acid (75 ml.) was hydrogenated overnight with a platinum catalyst. Working up in the usual way gave deoxyzeorin acetate, m. p. 200—202° (from chloroform–methanol), $[\alpha]_D$ +51° (*c*, 1·46), undepressed in m. p. on admixture with the specimen prepared as above.

Hydrolysis and benzoylation as in (*a*) above furnished deoxyzeorin benzoate, $[\alpha]_D$ +51° (*c*, 2·14), m. p. 233—234° undepressed on admixture with the benzoate reported in (a) above.

Deoxyzeorinone.—Deoxyzeorin acetate (500 mg.) was hydrolysed as for zeorin acetate (see above) and the crude deoxyzeorin oxidised in " AnalaR " acetic acid (20 ml.) by addition of chromium trioxide (200 mg.) in water (0·5 ml.) and acetic acid (15 ml.). After being left overnight at room temperature the product was crystallised from chloroform–methanol, to give *deoxyzeorinone*, m. p. 199—200°, $[\alpha]_D$ −6° (*c*, 2·01 in 2-dm. tube), $\lambda_{max.}$ 299 mμ (ε = 40) (Found : C, 84·0; H, 11·75. $C_{30}H_{50}O$ requires C, 84·45; H, 11·8%). This ketone was also prepared by chromic acid oxidation of the deoxyzeorin from the hydrogenation of *iso*zeorinin acetate. It then had m. p. 200—201° and gave no depression in m. p. with the ketone prepared by the alternative route.

epi*Deoxyzeorin*.—Deoxyzeorinone (750 mg.) in dry ether (100 ml.) was reduced by refluxing with a large excess of lithium aluminium hydride for 1 hour. The reaction product, isolated after working up in the usual way, was benzoylated with pyridine–benzoyl chloride at room temperature. After the customary treatment the benzoylated product was dissolved in

3 : 1 benzene–light petroleum. A crystalline compound, m. p. 275—285° (decomp.), $[\alpha]_D$ +6° (*c*, 2·34), slowly separated. It was not investigated further, but was removed by filtration. Chromatography of the filtrate over alumina gave *epideoxyzeorin*, eluted with 1 : 1 benzene–light petroleum and crystallised from chloroform–methanol; it had m. p. 208—209°, $[\alpha]_D$ −9° (*c*, 2·04) (Found: C, 84·0; H, 12·15. $C_{30}H_{52}O$ requires C, 84·05; H, 12·2%). This compound was saturated to tetranitromethane and showed no selective absorption in the ultraviolet region, even at 195—215 mμ.

*epi*Deoxyzeorin (50 mg.) was oxidised by chromium trioxide as in the oxidation of deoxyzeorin (see above). The product, after recrystallisation from chloroform–methanol, afforded deoxyzeorinone, $[\alpha]_D$ −5° (*c*, 1·09), m. p. 199—200° undepressed on admixture with authentic material (see above) of the same m. p.

Zeorinane.—(a) *Dehydration of deoxyzeorin with toluene-*p*-sulphonyl chloride.* Deoxyzeorin (200 mg.) was heated under reflux for 8 hours with toluene-*p*-sulphonyl chloride (400 mg.) in pyridine (3 ml.). After working up in the usual way, the product was filtered through alumina in light petroleum solution. Recrystallisation from chloroform–methanol gave a mixture of monounsaturated hydrocarbons, m. p. 157—159°, $[\alpha]_D$ −4° (*c*, 1·02) $\lambda_{max.}$ 199 mμ ($\varepsilon = 5000$; $\varepsilon_{215} = 800$) (*c*, 0·004) (Found: C, 87·4; H, 12·1. Calc. for $C_{30}H_{50}$: C, 87·75; H, 12·25%). Further recrystallisation did not change the m. p. or rotation {$[\alpha]_D$ −4° (*c*, 1·01 in 2-dm. tube)}.

This hydrocarbon mixture (100 mg.) was hydrogenated in ether–acetic acid overnight. After working up in the usual way and crystallisation from chloroform–methanol a mixture of saturated and unsaturated hydrocarbons resulted, having m. p. 147—148°, which then resolidified and remelted at 167—168°, and had $[\alpha]_D$ +13° (*c*, 0·95), +14° (*c*, 1·06), $\lambda_{max.}$ 198 mμ ($\varepsilon = 1900$; $\varepsilon_{215} = 300$) (*c*, 0·0044) (Found: C, 87·5; H, 11·9%). The mixture gave only a faint colour with tetranitromethane.

(b) *Pyrolysis of deoxyzeorin benzoate.* Deoxyzeorin benzoate (200 mg.) was heated in a small flask at 350° (bath-temp.) for 5 minutes *in vacuo*. The pyrolysis product was filtered through alumina in light petroleum and recrystallised from chloroform–methanol. After each crystallisation the m. p. remained constant at 157—158°, but the rotation increased steadily {2 recrysts., $[\alpha]_D$ +6° (*c*, 1·08); 3 recrysts., $[\alpha]_D$ +10° (*c*, 1·15); 4 recrysts., $[\alpha]_D$ +13° (*c*, 1·03); 5 recrysts., $[\alpha]_D$ +14° (*c*, 1·13)}. The final material gave no depression in m. p. with the mixture of unsaturated hydrocarbons (m. p. 157—159°), prepared as under (a) above. It showed $\lambda_{max.}$ 198 mμ ($\varepsilon = 3500$; $\varepsilon_{215} = 550$) (*c*, 0·004) and gave a distinct colour with tetranitromethane.

Hydrogenation of this mixture of hydrocarbons as under (a) above furnished a mixture of unsaturated and saturated hydrocarbons which, recrystallised from chloroform–methanol, had m. p. 150—151°, then resolidified and remelted at 167—168°, $[\alpha]_D$ +14° (*c*, 1·12), +14° (*c*, 1·10), $\lambda_{max.}$ 198 mμ ($\varepsilon = 3200$; $\varepsilon_{215} = 50$) (*c*, 0·0048), unchanged on further recrystallisation. The mixed m. p. with the corresponding mixture of hydrocarbons reported under (a) was undepressed and showed the same double m. p. The mixture gave only a faint colour with tetranitromethane.

(c) *Isolation of zeorinane.* The mixtures of saturated and unsaturated hydrocarbons reported in (a) and (b) above were dissolved in carbon tetrachloride (5 ml.) and acetic anhydride (0·5 ml.). Concentrated sulphuric acid (0·4 ml.) was then added dropwise with cooling. A further 0·5 ml. of acetic anhydride was added and the mixture left at room temperature for 30 minutes. After working up in the usual way the product was filtered in light petroleum solution through alumina. Once recrystallised from chloroform–methanol, it melted at 176—182°, gave no colour with tetranitromethane or with the Liebermann–Burchard reagent, and showed no maximum in the 195—215 mμ region ($\varepsilon < 25$).

This procedure was repeated on a larger scale (from 400 mg.) of deoxyzeorin, method (*a*) being used, and recrystallisation of the saturated hydrocarbon was continued until there was no further change in m. p. or rotation. This afforded *zeorinane*, m. p. 186·5—187·5°, $[\alpha]_D$ +12° (*c*, 1·00) (Found: C, 87·5; H, 12·6. $C_{30}H_{52}$ requires C, 87·3; H, 12·7%).

Dehydration of Zeorinin.—Zeorinin (100 mg.) was heated under reflux with toluene-*p*-sulphonyl chloride (200 mg.) in pyridine (3 ml.) for 9 hours. After working up in the usual way and filtration in light petroleum through alumina a hydrocarbon mixture was obtained which, recrystallised from chloroform–methanol, melted constantly at 150—151° and had $[\alpha]_D$ +55° (*c*, 1·15), +56° (*c*, 1·03) (Found: C, 88·1; H, 12·2. Calc. for $C_{30}H_{48}$: C, 88·15; H, 11·85%).

The mixture (50 mg.) was refluxed with "AnalaR" acetic acid (70 ml.) and concentrated hydrochloric acid (20 ml.) for 32 hours. Examination of the 215—300-mμ region gave no indication of selective butadienyl-type absorption in the crude reaction product.

Rearrangement of Zeorininone.—Zeorininone (400 mg.) was heated under reflux with dioxan (10 ml.) and concentrated hydrochloric acid (8 ml.) for 72 hours. After working up in the usual way, the product was crystallised repeatedly from chloroform–methanol, to give the highly crystalline neo*zeorininone*, m. p. 238—240°, $[\alpha]_D$ −2° (*c*, 1·05), −3° (*c*, 1·03), unchanged on further recrystallisation. This compound showed no high-intensity selective absorption in the 215—280-mμ region. It was not possible to detect the low-intensity saturated-ketone band in the 290-mμ region because of the sparing solubility of the ketone in ethanol. However, it showed $\lambda_{max.}$ 201 mμ ($\varepsilon = 9100$; $\varepsilon_{215} = 4900$) (*c*, 0·004) (Found: C, 84·0, 83·9; H, 11·1, 11·35. $C_{30}H_{48}O$ requires C, 84·85; H, 11·4%). *neo*Zeorininone was also obtained from an attempted Clemmensen reduction of zeorininone under the same conditions of acidity and reflux time (see Barton, Bruun, Fawcett, and Thomas, *J.*, 1951, 3154).

Preparation of hetero*Lupane.*—Taraxasterol was extracted from chamomile flowers by following the general directions of Burrows and Simpson (*J.*, 1938, 2042), except that it was found advantageous to use ether instead of carbon tetrachloride for the extraction. The crude taraxasterol was converted into the acetate and purified by chromatography over alumina. The acetate, recrystallised from chloroform–methanol, had m. p. 245—247°, $[\alpha]_D$ +100° (*c*, 1·37). The ester was hydrogenated in ether–acetic acid, to give taraxastanyl acetate which, recrystallised from chloroform–methanol, had m. p. 262—263°, $[\alpha]_D$ +16° (*c*, 2·06). For the latter compound Lardelli and Jeger (*Helv. Chim. Acta*, 1948, **31**, 813) recorded $[\alpha]_D$ +23°, but later the value of +19° was given (Lardelli, Krüsi, Jeger, and Ruzicka, *ibid.*, p. 1159). Alkaline hydrolysis of taraxastanyl acetate followed by chromic acid oxidation afforded taraxastanone which, recrystallised from chloroform–methanol, had m. p. 171—172°, $[\alpha]_D$ +42° (*c*, 2·77) (Lardelli and Jeger, *loc. cit.*, recorded $[\alpha]_D$ +45°). Wolff–Kishner reduction of the ketone and chromatography over alumina (elution with light petroleum) furnished *hetero*lupane which, recrystallised from chloroform–methanol, had m. p. 186—188°, $[\alpha]_D$ +11° (*c*, 2·17) (Found: C, 87·4; H, 12·5. Calc. for $C_{30}H_{52}$: C, 87·3; H, 12·7%). *hetero*Lupane gave a 30° m. p. depression on admixture with zeorinane (see above). *hetero*Lupane was recovered unchanged after treatment with acetic anhydride–sulphuric acid as in the Anderson–Nabenhauer procedure (see above).

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BIRKBECK COLLEGE, LONDON, W.C.1. [*Received, January 2nd*, 1952.]

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311. *Stability of Isomeric Butoxysilanes with Respect to Silicon Tetrachloride and Hydrogen Chloride.*

By W. GERRARD and J. V. JONES.

It is shown that disproportionation between the isomeric tetrabutoxysilanes (excluding the *tert.*-butoxy-compound) and silicon tetrachloride is very slow at the reflux temperature of the latter. In a sealed tube at 150° the *n*-butyl ester undergoes primary disproportionation into the tri- and the mono-chlorosilane; but in the same time the *iso*butyl and the *sec.*-butyl ester are scarcely affected. These esters show resistance to dealkylation by hydrogen chloride. Such observations are necessary for a detailed description of alcohol–silicon tetrachloride systems.

PRECISE description of the reaction sequences in alcohol–inorganic non-metallic halide systems requires detailed knowledge of the behaviour of the primarily liberated hydrogen halide and of the disproportionation tendencies of the relevant esters with respect to the original halide reagent. Disproportionation between tetra-alkoxysilanes and silicon tetrachloride has been listed as a method of preparation of chlorosilanes, because of the original observation by Friedel and Crafts (*Annalen*, 1863, **127**, 28; 1865, **136**, 203) who worked with methyl and ethyl homologues which were heated in a sealed tube at 160°.

Conditions for disproportionation in examples of the isomeric butyloxysilanes have now been determined. At the reflux temperature of silicon tetrachloride these tetra-esters (except that of *tert.*-butyl) showed no definite sign of disproportionation even after many hours. Whereas a trace of pyridine hydrochloride encouraged reaction of the *n*-butyl ester, it had no such obvious effect with the other two. The tetra-*n*-butyl ester suffered no definite disproportionation when heated with silicon tetrachloride in a sealed tube at 100° for 3 hours, but at 150° in the same time it underwent primary change into the tri- and the mono-chlorosilane. At 200° a secondary reaction would account for the dichlorosilane found. With the other two butyl tetra-esters, disproportionation at 150° was slow.

We believe that these effects are due to a screening of the silicon atom by alkyl groups which hinder the broadside four-centre approach of silicon tetrachloride, requiring a disposition in which the silicon of the tetrachloride approaches the oxygen atom of an alkyl-oxygen group, and at the same time a chlorine atom of the tetrachloride approaches the silicon atom of the tetra-ester. It is conceivable that hydrocarbon branching can cause more effective screening.

Dealkylation of the three tetra-esters by means of hydrogen chloride is evidently a slow process. Consideration of these data and those presented by Gerrard and Woodhead (*J.*, 1951, 519; *Research*, 1949, **2**, 48) for octan-2-ol shows that the silicon tetrachloride–alcohol system, in which the alcoholic carbon atom has what may be termed an " ordinary " degree of reactivity, entails simply a rapid stepwise dechlorination of the tetrachloride. If the addition of alcohol is stopped when one mol. of it has been added to one mol. of the tetrachloride, the trichlorosilane, $SiCl_3{\cdot}OR$, together with some dichlorosilane, $SiCl_2(OR)_2$, can be isolated; but further addition of alcohol will continue the formation of the dichlorosilane and develop the monochlorosilane as well, and ultimately the tetra-ester will tend to be formed. If, however, the tetrachloride is added dropwise to the alcohol, dechlorination is extensive by the time 0·25 mol. has been added, and further addition will merely delay the last stage of the dechlorination. We examined this point in some detail with *n*-butyl alcohol and found that the reaction mixture, resulting from the addition of 0·25 mol. of the tetrachloride to 1 mol. of alcohol, appeared to comprise the monochlorosilane (equivalent to about 0·75 mol. of alcohol) and alcohol (0·25 mol.) held in a state of comparative inactivity, presumably as ROH,HCl, for even after this mixture had been at 15° for an hour, it gave an approximately equivalent amount of the trichlorosilane on the continued addition of the tetrachloride, the main product being the monochlorosilane. When, however, the volatile matter was removed at 15°/15 mm. at the 0·25-mol. stage, tetra-*n*-butoxysilane was isolated whether or not more tetrachloride was added.

It is now clear why the tetra-ester is formed rapidly and completely when the tetrachloride is added to the alcohol in the presence of pyridine. Furthermore, it may be concluded that, apart from interaction between hydrogen chloride and alcohol, silicon tetrachloride–alcohol systems entail no reaction sequence which proceeds sufficiently quickly to lead to ordinarily perceptible amounts of alkyl chloride.

The situation is very different when the alcoholic carbon atom is much more reactive, *e.g.*, in 1-phenylethanol, which very rapidly gave 1-chloro-1-phenylethane in high yield when mixed with the tetrachloride (Gerrard and Woodhead, *loc. cit.*). Furthermore, tetra-(1-phenylethoxy)silane was readily and completely dealkylated by hydrogen chloride, the alkyl chloride being isolated in high yield.

These observations are now available for comparison with those on the alcohol–phosphorus halide systems (Gerrard, *J.*, 1940, 1464; 1944, 85; 1945, 106; 1946, 741) and with those on the alcohol–boron trichloride systems (Gerrard and Lappert, *J.*, 1951, 1020, 2545; cf. also the zirconium alkoxides, Bradley and Wardlaw, *J.*, 1951, 820).

Experimental

The tetra-alkyloxysilanes were prepared by addition of silicon tetrachloride (1 mol.) to a mixture of the alcohol (4 mols.) and pyridine (4 mols.) in pentane as described by Gerrard and Woodhead (*loc. cit.*).

Disproportionation Experiments.—(a) *At reflux temperature.* Tetra-*n*-butoxysilane, b. p. 106°/0·4 mm., d_{20}^{20} 0·897, n_D^{20} 1·4138 (Found: C, 60·6; H, 11·25. Calc. for $C_{16}H_{36}O_4Si$: C, 60·0;

H, 11·25%) (8 g., 1 mol.) was mixed with silicon tetrachloride (freshly distilled; 17 g., 4 mols.) and heated at the reflux temperature of the latter for 12 hours. The tetrachloride (14·7 g.), b. p. 57—60°, and the tetra-ester (7·8 g.), b. p. 127°/1·5 mm. [redistilled (7·3 g.), b. p. 107°/0·5 mm., n_D^{20} 1·4140], were recovered. There was a primary residue (0·5 g.). The same quantities of materials after being heated at reflux temperature for 10 hours a day for 8 days afforded the tetrachloride (14·5 g.), b. p. 57—60°, the tetra-ester (7·1 g.), b. p. 104°/0·3 mm., n_D^{20} 1·4139, and a residue (0·8 g.).

Tetra*iso*butoxysilane, b. p. 90°/0·4 mm., d_{20}^{20} 0·886, n_D^{20} 1·4090 (Found: C, 60·4; H, 11·28%) (8·0 g., 1 mol.), and the tetrachloride (17 g., 4 mols.) were similarly heated for 12 hours. The tetra-ester (7·3 g.), b. p. 90°/0·2 mm., n_D^{20} 1·4090, was recovered.

Tetra-*sec.*-butoxysilane, b. p. 87°/2 mm., d_{20}^{20} 0·883, n_D^{20} 1·4070 (Found: C, 60·2; H, 11·26%) (8·0 g., 1 mol.), and the tetrachloride (17 g., 4 mols.) were similarly heated for 12 hours. The tetra-ester (7·6 g.), b. p. 84—87°/1·5 mm., was recovered.

When undistilled silicon tetrachloride (containing traces of chlorides of iron, titanium, and aluminium) was used instead of the purified material, the *n*-butoxysilane was again recovered as described. Pyridine hydrochloride (0·2 g., 0·05 mol.; for 1 mol. of tetra-ester and 4 mols. of tetrachloride) facilitated disproportionation. After 12 hours at reflux temperature tetra-*n*-butoxysilane (8·0 g.) afforded a liquid (5·5 g.), b. p. 100—120°/15 mm., and another (4·0 g.), b. p. 120—130°/15 mm., there being a small residue (0·4 g.). From the first liquid a fairly pure specimen of di-*n*-butoxydichlorosilane (3·0 g.), b. p. 95—105°/15 mm. (Found: Cl, 28·1. Calc. for $C_8H_{18}O_2Cl_2Si$: Cl, 28·9%), was obtained together with a liquid (2·4 g.), b. p. 105—120°/15 mm. (Found: Cl, 19·7%), which was probably a mixture of the di- and mono-chlorosilane. The liquid of b. p. 120—130°/15 mm. afforded tri-*n*-butoxychlorosilane (2·1 g.), b. p. 120—125°/15 mm. (Found: Cl, 13·0. Calc. for $C_{12}H_{27}O_3ClSi$: Cl, 12·5%), and a further fraction (1·7 g.), b. p. 125—130°/12 mm. (Found: Cl, 6·2%). The base hydrochloride has no such decided influence with the tetra-*iso*- or -*sec.*-butyl esters: the former afforded impure tetra-ester (4·5 g.), b. p. 79—81°/0·4 mm. (Found: Cl, 1%), and a better specimen (2·8 g.), b. p. 82—85°/0·3 mm., n_D^{20} 1·4088, and the *sec.*-butyl ester was largely recovered (7·5 g.), b. p. 77—79°/0·3 mm., n_D^{20} 1·4065.

(b) *In a sealed tube.* Tetra-*n*-butoxysilane (4·0 g.) and the tetrachloride (8·5 g.) were heated in a sealed tube for 3 hours at 200°. The tetrachloride (4·2 g.), b. p. 57—80° (Found: Cl, 82·9. Calc.: Cl, 83·4%), and the following fractions were obtained: *A* (0·8 g.), b. p. 80—100°; *B* (2·5 g.), b. p. 75—105°/57—60 mm.; *C* (2·4 g.), b. p. 110—135°/16 mm.; *D* (0·8 g.), b. p. 75—85°/0·2 mm., and a residue (0·3 g.). Fraction *B* afforded *n*-butoxytrichlorosilane (2·15 g.), b. p. 67—74°/50 mm. (Found: Cl, 50·5; Si, 13·25. Calc. for $C_4H_9OCl_3Si$: Cl, 51·25; Si, 13·5%), and *C* gave impure di-*n*-butoxydichlorosilane (0·7 g.), b. p. 103—110°/13 mm. (Found: Cl, 25·7. Calc. for $C_8H_{18}O_2Cl_2Si$: Cl, 28·9%), a middle fraction (0·3 g.), b. p. 110—128°/13 mm., and tri-*n*-butoxychlorosilane (0·8 g.), b. p. 128—131°/13 mm. (Found: Cl, 13·0. Calc. for $C_{12}H_{27}O_3ClSi$: Cl, 12·55%). Purification of these distillates was not carried further. Repetition at 150° afforded a fraction *A* (1·9 g.), b. p. 60—90°/60 mm., from which *n*-butoxytrichlorosilane (1·6 g.), b. p. 67—69°/48 mm. (Found: Cl, 51·5%), was obtained, and a fraction *B* (3·5 g.), b. p. 100—145°/15 mm., from which tri-*n*-butoxychlorosilane (2·9 g.), b. p. 128—133°/15 mm. (Found: Cl, 12·2%), was obtained.

Repetition at 100°, however, gave mainly tetra-*n*-butoxysilane (3·5 g.), b. p. 106—108°/0·5 mm., n_D^{20} 1·4140.

By the same process and with the same quantities of materials kept at 150° for 3 hours, tetra*iso*butoxysilane afforded two fractions; *A* (1·8 g.), b. p. 69—75°/0·1 mm. (Found: Cl, 2·4%), and *B* (2·0 g.), b. p. 75—82°/0·1 mm. (Found: Cl, 1·9%), and a residue (0·3 g.). Similarly, tetra-*sec.*-butoxysilane afforded silicon tetrachloride (7·0 g.) and contaminated tetra-ester (3·8 g.), b. p. 78—80°/0·3 mm. (Found: Cl, 1%), there being a residue (0·2 g.).

*Interaction of Hydrogen Chloride and Tetra-*n*-butoxysilane.*—Dry hydrogen chloride was passed into the tetra-ester (8·0 g.) for 3 hours at 20°, and the final increase in weight was 0·7 g., corresponding to 0·77 mol. of the gas for 1 mol. of ester. After dry air had been passed through the liquid, the weight (8·05 g.) was almost that of the ester used. On distillation the tetra-ester (7·3 g.), b. p. 95—105°/0·4 mm., and a brown gelatinous residue (0·6 g.) were obtained, and on redistillation, the tetra-ester (7·0 g.), b. p. 101°/0·4 mm., and a residue (0·3 g.). During the approach to distillation temperature and during the passage of gas, a U-tube, cooled at −80°, was attached to the exit tube from the apparatus. No more than a trace of liquid was so collected.

When the gas was passed into the ester at 55° for 3 hours, the increase in weight was 0·1 g.

(0·12 mol.), but the weight returned to 8·0 g. on passage of dry air. From the residue, *n*-butyl alcohol (0·3 g.), b. p. 60—65°/20 mm., d_{20}^{20} 0·810, the tetra-ester (7·1 g.), b. p. 108—113°/1·0 mm., and a brown gelatinous residue (0·5 g.) were obtained. On redistillation, the tetra-ester (6·8 g.), b. p. 95—96°/0·15 mm., and a residue (0·3 g.) were obtained.

Similarly at 20° tetra-*sec.*-butoxysilane (8·0 g.) absorbed 0·5 g. (0·55 mol.) of gas, but most of this was removed in a stream of air. From the residue, the tetra-ester (7·0 g.), b. p. 65—83°/0·3 mm., and a brown gelatinous residue (0·6 g.) were obtained, and on redistillation of the ester fraction, the ester (6·6 g.), b. p. 66—70°/0·05 mm., and a residue (0·4 g.).

Dechlorination of Silicon Tetrachloride by n-*Butyl Alcohol.*—Silicon tetrachloride (9·4 g., 1·1 mols.) in *n*-pentane (15 c.c.) was added dropwise (30 minutes) with shaking to the alcohol (14·8 g., 4 mols.) in pentane (20 c.c.) at −10°. Evolution of hydrogen chloride soon began and, when mixing was complete, dry air was passed (10 minutes) to sweep away most of the gas. Easily volatile matter was removed at 20°/15 mm. (20 minutes), and distillation then afforded tetra-*n*-butoxysilane (15·2 g., 95%), b. p. 92—97°/0·4 mm., and a residue (0·3 g.). On redistillation, the tetra-ester (14·8 g.), b. p. 99—101°/0·5 mm., n_D^{20} 1·4140, and a residue (0·4 g.) were obtained.

Similar addition of the tetrachloride (34 g., 4 mols.) (45 minutes) followed by removal of volatile matter at 15°/15 mm. (1 hour) and distillation afforded crude *n*-butoxytrichlorosilane (3·3 g.), b. p. 82—95°/45 mm. [redistilled (2·5 g.), b. p. 70—75°/45 mm. (Found: Cl, 50·0. Calc. for $C_4H_9OCl_3Si$: Cl, 51·25%)], and crude tri-*n*-butoxychlorosilane (17·4 g.), b. p. 65—70°/0·1 mm. [redistilled (16·8 g.), b. p. 65—67°/0·1 mm. (Found: Cl, 12·5. Calc. for $C_{12}H_{27}O_3ClSi$: Cl, 12·5%)]. There was a residue (0·6 g.) from the primary distillation. It will be noticed that in this experiment the tetrachloride was added about three times as fast as in the first experiment, and furthermore, addition was continued without interruption to the stage of 1 mol. of reagent for 1 mol. of alcohol. Now when the process was interrupted at the 0·25-mol. stage (tetrachloride, 4·25 g.; alcohol, 7·4 g.) (time of addition, 20 minutes) in order to remove volatile matter at 15°/15 mm., and then the tetrachloride (12·75 g., 0·75 mol.) (in pentane, 15 c.c.) was added to the residue (30 minutes), distillation, after the usual removal of volatile matter at 15°/15 mm., afforded tetra-*n*-butoxysilane (7·5 g.), b. p. 95—105°/0·3 mm. [redistilled (7·2 g.), b. p. 102—104°/0·3 mm., n_D^{20} 1·4138]. There was a residue (0·5 g.) from the first distillation. In a final experiment, the addition was again interrupted at the 0·25-mol. stage, but this time the mixture was merely kept for 1 hour at 15° and then cooled at −10° whilst the remainder (12·75 g., 0·75 mol.) of the tetrachloride was added (30 minutes). After volatile matter had been removed at 15°/15 mm., crude trichlorosilane (1·2 g.) (from alcohol, 7·4 g.), b. p. 60—75°/30 mm., an intermediate fraction (0·3 g.), b. p. 75—130°/30 mm., and monochlorosilane (8·6 g.), b. p. 70—90°/0·2 mm. [redistilled (8·2 g.), b. p. 73—77°/0·2 mm. (Found: Cl, 12·8%)], were obtained. There was a residue (0·4 g.), and redistillation of the first fraction (1·2 g.) afforded a good specimen of the trichlorosilane (1·0 g.), b. p. 58—64°/33 mm. (Found: Cl, 50·3%).

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312. *The Determination of C-Methyl Groups in Some Branched-chain Fatty Acids.*

By A. D. CAMPBELL and (MISS) J. E. MORTON.

By using compounds of known constitution it has been found that the Kuhn–Roth method (Ginger's modification) for the estimation of *C*-methyl groups gives one mole of acetic acid (62—99% yield) for each $-CMe_3$, $>CMe_2$, and $\gtrless$CMe group. The method therefore cannot be used as a means of determining for certain the number of methyl groups present in the molecule or their particular nature.

THE Kuhn–Roth procedure for the determination of *C*-methyl groups (Kuhn and Roth, *Ber.*, 1933, **66**, 1274) has been accepted by various workers since it was introduced in 1933. It involves oxidation of the compound by chromic acid to give, theoretically, one mole of acetic acid for every *C*-methyl group per mole of compound.

Kuhn and Roth describe the determination of *C*-methyl groups in a number of complex materials some of which contain *gem*-dimethyl groups. Examination of this original work, however, indicates that the method was tested on complex compounds containing both *gem*-dimethyl and $\geqslant$CMe groups. Lycopene, for example, which contains six $\geqslant$CMe groups as well as two $>CMe_2$ groups gives acetic acid for six *C*-methyl groups in 91% yield or for eight in 69% yield. As the yield of acetic acid varies considerably and may be as low as 62%, analysis of such compounds will not show whether the acetic acid comes from the $\geqslant$CMe groups alone or from both $\geqslant$CMe and $>CMe_2$ groups.

The exact behaviour of the $>CMe_2$ and $-CMe_3$ groups in particular requires elucidation because Milton and Waters (" Methods of Quantitative Microanalysis," E. Arnold & Co., 1949, p. 111) state that $>CMe_2$ and $-CMe_3$ groups yield acetone. The purpose of the work now reported has been to determine the reaction of *gem*-dimethyl and *tert.*-butyl groups and certain other types of side chains in compounds submitted to the Kuhn–Roth procedure as modified by Ginger (*J. Biol. Chem.*, 1944, **156**, 452). Our results are tabulated.

Substance	AcOH, moles per mole of compound	
1, Decanoic acid	0·99	1 Me in 99% yield
2, Stearic acid	0·96	1 ,, 96% ,,
3, *iso*Valeric acid	0·78	1 ,, 78% ,,
	* 0·84	1 ,, 84% ,,
4, 2-*n*-Butylhexanoic acid †	1·64	2 ,, 82% ,,
5, Pivalic acid	0·72	1 ,, 72% ,,
6, 2 : 2-Dimethyloctanoic acid †	1·64	2 ,, 82% ,,
7, α-Methyl-α-*n*-propylvaleric acid	2·10	3 ,, 70% ,,
8, α-Ethyl-α-*n*-propylvaleric acid	1·86	3 ,, 62% ,,
9, αα-Diethylvaleric acid	1·86	3 ,, 62% ,,
10, 4 : 4-Dimethyltetradecanoic acid †	1·70	2 ,, 85% ,,
	1·90	2 ,, 95% ,,
11, 3-Methylbutan-2-one	* 1·62	2 ,, 81% ,,
	1·68	2 ,, 84% ,,
12, Mesityl oxide	* 1·54	2 ,, 77% ,,
13, Acetone	* 0·74	1 ,, 74% ,,

* Acetic acid identified as its *p*-bromophenacyl ester. † Geneva convention, $CO_2H = 1$.

The relatively high yield of acetic acid found on oxidation of $>CMe_2$ groups (compounds **3**, **6**, **10**, **11**, **12**) and $-CMe_3$ groups (compound **5**) precludes the formation of acetone under the conditions used. Acetone itself underwent oxidation to acetic acid in 74% yield even although there is the possibility of loss owing to volatility. It was thought that mesityl oxide, owing to its structure, would oxidise readily to give acetone but acetic acid was obtained for the $>CMe_2$ and $\geqslant$CMe groups in 77% yield. It is thus clear that $>CMe_2$ and $-CMe_3$ groups give acetic acid and not acetone.

Duplicate analyses (see table) were fairly reproducible. However, Cason and Sumrell (*ibid.*, 1951, **192**, 411) state that their microanalyst " was unable to obtain satisfactorily consistent results by the method of Ginger." By digesting the fatty acids at 120° in a sealed tube for 11—14 hours reasonably consistent results (75—90% yield) were obtained on synthetic branched-chain acids but even with this modification it is reported that some analyses gave very low results. In the present work, with digestions at 100°, the only two compounds to give less than a 70% yield of acetic acid per group were two acids of similar structure each containing three $\geqslant$CMe groups.

No conclusive evidence of the amount of branching in a chain can be obtained by the Kuhn–Roth method, as the results show that the acid could come from a $\geqslant$CMe, $>CMe_2$, or $-CMe_3$ group. Also, as the yield of acetic acid may be as low as 60% in branched-chain compounds, if more than three *C*-methyl groups are present then the results cannot be interpreted with any degree of certainty.

Experimental.—*C*-Methyl determinations on 10—20-mg. samples of the compounds listed were carried out in the micro-acetyl apparatus described by Pregl (transl. Grant, " Quantitative Organic Microanalysis," J. & A. Churchill Ltd., 1945, p. 162). Ginger's modification was used except that all samples were digested for 1½—2 hours by immersing the reaction flask deeply in a

boiling-water bath. In cases indicated in the table the acetic acid in the distillate was identified as the *p*-bromophenacyl ester.

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313. *Studies of Trifluoroacetic Acid. Part V.* Trifluoroacetic Anhydride as a Condensing Agent in Reactions of Nitrous and Nitric Acids.*

By E. J. BOURNE, M. STACEY, J. C. TATLOW, and J. M. TEDDER.

IN earlier papers in this series (*J.*, 1949, 2976; *J.*, 1951, 718) it has been shown that mixtures of trifluoroacetic anhydride and carboxylic acids react with hydroxy-compounds and with activated aromatic compounds to give esters and ketones, respectively, and that trifluoroacetic anhydride–sulphonic acid mixtures behave in an analogous fashion to yield sulphonic esters and sulphones. A mechanism for these reactions was advanced recently by Bourne, Randles, Tatlow, and Tedder (*Nature*, 1951, **168**, 942). We have now shown that, as was expected, solutions of fuming nitric acid in trifluoroacetic anhydride can be used to synthesise nitrate esters from polyhydric alcohols and nitro-derivatives from aromatic compounds, including those possessing deactivating groups. For the nitration of cyanides, these solutions offer an advantage over the usual nitric–sulphuric acid nitrating mixture inasmuch as they cause negligible hydrolysis.

It was expected that solutions of alkyl nitrites in trifluoroacetic anhydride would introduce nitroso-groups into aromatic compounds; the direct introduction of such groups by accepted methods can be achieved usually only in the cases of phenols and tertiary amines. However, in place of the nitroso-derivatives, nitro-compounds, diazonium salts, and unidentified nitrogenous syrups were produced. With the less reactive aromatic compounds (*e.g.*, benzene and naphthalene), nitration was the predominant reaction, but diazonium salts (isolated as azo-dyes) were the main products from the more reactive aromatic compounds (*e.g.*, mesitylene, ψ-cumene, and anisole). Toluene and *o*-xylene gave only traces of diazonium salts. Improved yields of the diazonium salts resulted when nitroso-compounds were treated in the same way. Thus, it is probable that solutions of nitrites in trifluoroacetic anhydride do, in fact, function as nitrosating agents, but that the nitroso-compounds formed initially are subsequently converted into diazonium salts. A plausible explanation of the second stage is that dehydration of the nitrite gives dinitrogen trioxide, and thence, by disproportionation, nitric oxide and nitrogen dioxide, for it was demonstrated by Bamberger (*Ber.*, 1897, **30**, 512; 1918, **51**, 634) that nitroso-compounds and nitric oxide form diazonium nitrates:

$$R{\cdot}NO + 2NO \longrightarrow R{\cdot}N_2^+ NO_3^-$$

Whilst the results of the above nitrations and nitrosations accord with the hypothesis of Bourne, Randles, Tatlow, and Tedder (*loc. cit.*), developed for carboxylic acids, that the reactive entity present in mixtures of the oxy-acid XOH and trifluoroacetic anhydride is the ion X^+, it does not necessarily follow that the implied mechanism is correct for oxy-acids of nitrogen (cf. Hughes, Ingold, *et al.*, *J.*, 1950, 2400 *et seq.*).

Experimental.—Nitration of phenyl cyanide. A mixture of phenyl cyanide (0·50 c.c.), fuming nitric acid (0·80 c.c.), and trifluoroacetic anhydride (1·50 c.c.) was kept at 55° for 90 minutes, cooled, and poured into excess of aqueous sodium hydrogen carbonate. Extraction with chloroform, evaporation of the extracts, and recrystallisation of the residue from acetone–

* Part IV, *J.*, 1951, 826.

light petroleum (b. p. 40—60°) gave *m*-nitrophenyl cyanide (85%), m. p. 117° (Found: C, 56·7; H, 2·8. Calc. for $C_7H_4O_2N_2$: C, 56·8; H, 2·7%). Bogert and Beans (*J. Amer. Chem. Soc.*, 1904, **26**, 464) recorded m. p. 117—117·5°. Ethereal extracts of the acidified aqueous layer afforded *m*-nitrobenzoic acid (1%).

A similar reaction, in which trifluoroacetic anhydride was replaced by concentrated sulphuric acid (0·50 c.c.), gave *m*-nitrophenyl cyanide and *m*-nitrobenzoic acid, the yields being 40 and 45%, respectively.

Other nitrations. In two similar experiments with trifluoroacetic anhydride, nitrobenzene gave *m*-dinitrobenzene (65%), and bromobenzene afforded the *o*-nitro- (1%), the *p*-nitro- (24%), and the 2 : 4-dinitro-derivative (60%). Mannitol and sorbitol, nitrated at 0°, gave the corresponding hexanitrates (45%).

Mesitylazo-β-naphthol. Amyl nitrite (2·20 c.c.) was added slowly, at 0°, to a mixture of mesitylene (0·40 c.c.) and trifluoroacetic anhydride (4·30 c.c.); a deep brown colour developed rapidly. After being kept at 0° for 2 hours, the whole was poured into crushed ice and excess of sodium hydrogen carbonate, and extracted with ether. The aqueous layer was treated with excess of β-naphthol in sodium hydroxide. The azo-dye was extracted with chloroform. Recrystallised from aqueous acetone, the product gave bright red needles of *mesitylazo-β-naphthol* (0·39 g., 47%), m. p. 131—133° (Found: C, 78·3; H, 6·2. $C_{19}H_{18}ON_2$ requires C, 78·6; H, 6·2%).

In a second experiment, mesitylene (0·40 c.c.) was treated with ethyl nitrite (1·50 c.c.) and trifluoroacetic anhydride (2·00 c.c.) at 0° for 20 minutes, and the azo-dye was obtained in 47% yield, having m. p. 130—131°.

2 : 4 : 5-*Trimethylphenylazo-β-naphthol.* A mixture of trifluoroacetic anhydride (2·10 c.c.), ψ-cumene (0·50 c.c.), and amyl nitrite (1·60 c.c.) was treated as above. Recrystallised from aqueous acetone, the azo-dye (0·15 g., 13%) had m. p. 159° (Found: C, 78·9; H, 6·2. Calc. for $C_{19}H_{18}ON_2$: C, 78·6; H, 6·2%). Charrier and Ferreri (*Gazzetta*, 1914, **44**, 120) reported m. p. 160—161°.

p-*Methoxyphenylazo-β-naphthol.* A mixture of trifluoroacetic anhydride (1·90 c.c.), anisole (0·36 c.c.), and ethyl nitrite (1·40 c.c.) was kept at 0° for 20 minutes, mixed with ice and excess of sodium hydrogen carbonate solution, and treated with β-naphthol as reported above. Recrystallised from aqueous acetone, the product gave *p*-methoxyphenylazo-β-naphthol (0·19 g., 21%), m. p. 139—140° (Found: C, 73·4; H, 4·8. Calc. for $C_{17}H_{14}O_2N_2$: C, 73·4; H, 5·1%). Koch, Milligan, and Zuckerman (*Ind. Eng. Chem., Anal.*, 1944, **16**, 755) gave m. p. 140—141°.

Phenylazo-β-naphthol from nitrosobenzene. Nitrosobenzene (0·15 g.) was added, at 0°, to a mixture of amyl nitrite (0·40 c.c.) and trifluoroacetic anhydride (0·80 c.c.), which had been kept previously at 40° for 5 minutes. After 1 hour at 0°, the reaction mixture was treated with ice and excess of sodium hydrogen carbonate solution, and the azo-dye was prepared in the usual fashion. The product, recrystallised from acetic acid, gave dark red needles (0·16 g., 48%), m. p. 131°. Koch, Milligan, and Zuckerman (*loc. cit.*) reported m. p. 131—132°.

Mesitylazo-β-naphthol from nitrosomesitylene. A mixture of nitrosomesitylene (0·074 g.), amyl nitrite (0·30 c.c.), and trifluoroacetic anhydride (0·50 c.c.) was kept at 0° for 1 hour, and treated with β-naphthol as before. The product (0·087 g., 60%) had m. p. 130°, alone or on admixture with mesitylazo-β-naphthol.

1-*Nitronaphthalene.* A mixture of trifluoroacetic anhydride (0·70 c.c.), amyl nitrite (0·40 c.c.), and naphthalene (0·15 g.) was kept at 0° for 3 hours, poured into excess of sodium hydrogen carbonate solution, and extracted with chloroform; the extracts were dried ($MgSO_4$), filtered, and evaporated, leaving a solid residue, which, when recrystallised from aqueous alcohol, gave 1-nitronaphthalene (0·16 g., 79%), m. p. 61° alone or on admixture with an authentic specimen. When the aqueous layer resulting from the chloroform extraction was treated with β-naphtho' no azo-dye was formed.

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CHEMISTRY DEPARTMENT, THE UNIVERSITY,
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314. *Andrographolide. Part I.*

By (Mrs.) D. Chakravarti and R. N. Chakravarti.

Contrary to observations by Guha-Sircar and Moktader, andrographolide does not contain a methylenedioxy-group; Gorter's original findings that andrographolide is a trihydroxy-lactone, with one tertiary hydroxy-group, have been established. Hydrogenation of andrographolide in acetic acid solution with Adams's catalyst furnishes two isomeric deoxytetrahydroandrographolides, indicating the presence of two double bonds. Hydrogenation in methanolic solution in presence of palladium leads to the same mixture of isomers; Guha-Sircar and Moktader's claim to have isolated a dihydroandrographolide under these conditions was not substantiated. That andrographolide is an αβ-unsaturated lactone is evident from ultra-violet absorption spectra and a positive Legal test. Elimination of a molecule of formaldehyde during ozonolysis indicates the presence of a methylene group attached to a double bond.

Andrographis paniculata Nees (Bengali, Kalmegh) grows widely throughout the plains of India. Its extremely bitter leaves form the chief constituent of a household medicine, "*Alui*," extensively used in Bengal in cases of bowel complaints of children and as a febrifuge and anthelmintic. According to Chopra ("Indigenous Drugs of India," Art Press, Calcutta, 1933, p. 280), as a bitter it is in no way inferior to other bitters mentioned in pharmacopœias.

Pure crystalline andrographolide, the bitter constituent of this plant, was first isolated by Gorter (*Rec. Trav. chim.*, 1911, **30**, 151; 1914, **33**, 239). According to him it is a trihydroxy-lactone, $C_{20}H_{30}O_5$, with one tertiary hydroxy-group. Later, Guha-Sircar and Moktader (*J. Indian Chem. Soc.*, 1939, **16**, 333) failed to prepare Gorter's triacetylandrographolide but obtained evidence indicating the presence of a methylenedioxy-group and a hydroxy-group in andrographolide instead of three hydroxy-groups.

The present authors have confirmed Gorter's original findings mentioned above. Contrary to observations by Guha-Sircar and Moktader (*loc. cit.*) it gives no formaldehyde on distillation with 33% sulphuric acid and does not appear to contain a methylenedioxy-group: it does not respond to Gabel's test or give a green colour with gallic acid and concentrated sulphuric acid. On the other hand, as a trihydroxy-compound, under conditions described in the Experimental section, it furnishes the triacetate which Guha-Sircar and Moktader failed to prepare. We have also substantiated Gorter's observation that this triacetyl derivative on reduction with aluminium amalgam in presence of moist ether affords diacetyldeoxyandrographolide, $C_{20}H_{28}O_2(OAc)_2$, indicating that one of the three hydroxy-groups is tertiary.*

Contrary to Guha-Sircar and Moktader's statements, andrographolide smoothly reduces ammoniacal silver nitrate and cold potassium permanganate. When subjected to the Legal test under the modified conditions described by Paist, Blout, Uhle, and Elderfield (*J. Org. Chem.*, 1941, **6**, 273) it appears to contain an αβ-unsaturated lactone system. This is confirmed by the ultra-violet absorption spectrum. In this respect it is similar to the other physiologically active unsaturated lactones occurring in Nature.

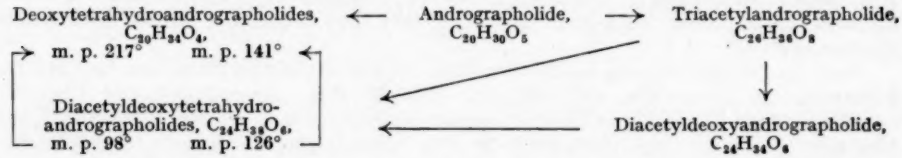
Hydrogenation of andrographolide in acetic acid solution in presence of Adams's catalyst leads to two isomeric deoxytetrahydroandrographolides, $C_{20}H_{34}O_4$, indicating the presence of two double bonds and a labile hydroxy-group which is eliminated. This further supports Gorter's observation (*loc. cit.*) that andrographolide contains a tertiary hydroxy-group.

* A short communication containing all the findings described in the present paper was submitted on 15th September, 1950, and appeared in the Proceedings of the 38th Indian Science Congress, 1951, Part III, Abstracts, p. 79. Most of the findings have since been confirmed by Schwyzer, Biswas, and Karrer (*Helv. Chim. Acta*, 1951, **34**, 652). No reference was, however, made in the latter paper to our findings which have priority.

The same products are obtained by carrying out the hydrogenation in methanolic solution (acidic) in presence of palladium chloride although Guha-Sircar and Moktader (*loc. cit.*) could only isolate a dihydroandrographolide under these conditions. Thus, also with palladium hydrogenolysis of the tertiary hydroxy-group takes place.*

The presence of two double bonds, three hydroxy-groups and the lactone system having been established, the molecule should contain two homocyclic rings.

Alkaline hydrolysis of a mixture (m. p. 175°) of the two isomers of deoxytetrahydroandrographolide, as obtained by hydrogenation of triacetylandrographolide followed by hydrolysis, affords a single crystalline product, deoxytetrahydroandrographolic acid, $C_{20}H_{36}O_5$, m. p. 107—108°. Gorter isolated diacetyldeoxytetrahydroandrographolide, m. p. 90—91°, by hydrogenation of diacetyldeoxyandrographolide in acetic acid solution in presence of platinum black. It has now been possible to isolate from this product two isomers, m. p. 126° and m. p. 98° respectively. Under similar conditions triacetylandrographolide absorbs three mols. of hydrogen with the formation of the same mixture of isomers of diacetyldeoxytetrahydroandrographolide, indicating loss of the acetoxy-group corresponding to the tertiary hydroxy-group. None of these deoxy-compounds gives a red colour with methanolic potassium hydroxide which is a characteristic test for andrographolide and its derivatives containing the tertiary hydroxy-group. On deacetylation the higher-melting diacetyldeoxytetrahydroandrographolide gives the lower-melting deoxytetrahydroandrographolide, the higher-melting isomer of which is obtained by the deacetylation of the product, m. p. 98°, described above (cf. scheme).



When andrographolide is ozonised in acetic acid solution and the product is distilled in steam, formaldehyde is isolated in almost quantitative yield as the 2 : 4-dinitrophenylhydrazone; a second ketone was isolated, but in quantity too small for further work.

Experimental

Analyses by Dr. G. Weiler and Dr. F. B. Strauss, of Oxford.

Large quantities of andrographolide required for this work were obtained by extraction of the air-dried leaves of *Andrographis paniculata* with boiling chloroform in a Soxhlet extractor as described by Guha-Sircar and Moktader (*loc. cit.*). The crude light green product obtained in this way was purified by crystallisation from methanol, separating in large colourless prisms, m. p. 228° (frothing). Andrographolide prepared by Gorter had m. p. 218°. The seasona variation in andrographolide contents of this annual plant is considerable. An average yield above 2% of the air-dried material can be obtained if the leaves are collected in October—November just before flowering. The yield drops to less than 0·5% after January, when the leaves also become very scarce. The stems of the plant also contain sufficient amounts of the bitter principle and the concentration in the stems runs parallel to that in the leaves. The root and seeds of this plant do not appear to contain andrographolide.

Andrographolide (Found : C, 68·4; H, 8·7. Calc. for $C_{20}H_{30}O_5$: C, 68·5; H, 8·6%) reduces potassium permanganate solution in the cold and ammoniacal silver nitrate on gentle heating. When treated with sodium nitroprusside under conditions for the Legal test as modified by

* It appears the tertiary hydroxy-group is eliminated when the hydrogenation is carried out in an acidic medium, three mols. of hydrogen being absorbed. Schwyzer *et al.* (*loc. cit.*) carried out the hydrogenation in neutral medium (ethanolic solution in presence of Adams's catalyst) but in this case total absorption represented two mols. and the product isolated was tetrahydroandrographolide, $C_{20}H_{34}O_5$, m. p. 180—188°. This has been confirmed by the present authors although the product had a higher m. p. The hydrogenation was carried out by shaking a solution of andrographolide (0·5 g.) and platinum oxide (50 mg.) in absolute ethanol (30 c.c.) in an atmosphere of pure hydrogen. Absorption, complete in 45 minutes, represented two mols. of hydrogen. After several crystallisations the product had m. p. 213—214° (Found : C, 68·0; H, 9·6. Calc. for $C_{20}H_{34}O_5$: C, 67·8; H, 9·6%).

Elderfield *et al.* (*loc. cit.*) it shows an intense purple-red colour which deepens and then fades. The ultra-violet absorption spectrum shows a maximum at 220 mμ (log ε = 4·1 in absolute ethanol). On distillation with 33% sulphuric acid it does not split off formaldehyde.

Triacetylandrographolide.—A mixture of andrographolide (0·1 g.), freshly distilled acetic anhydride (0·5 c.c.), and a minute quantity of fused zinc chloride was heated to about 90° till a clear solution was obtained (about 5 minutes). The solution was cooled, treated with water (1 c.c.), and shaken vigorously. A heavy oil separated which gradually solidified. Triacetylandrographolide crystallises from ethanol in silky needles, m. p. 128° (yield, almost quantitative) (Found: C, 65·8; H, 7·4. Calc. for $C_{26}H_{36}O_8$: C, 65·5; H, 7·5%).

Diacetyldeoxyandrographolide.—A solution of triacetylandrographolide (0·6 g.) in ether was added to aluminium amalgam (prepared from 3·6 g. of aluminium foil) immersed in ether (300 c.c.). Water, in small quantities, was added to this mixture during about 3 hours, the end of the reduction being indicated when the product gave no red colour with methanolic potassium hydroxide. The ethereal solution was then washed with water and the ether evaporated off. The residue, on crystallisation from ethanol, separated as flat needles, m. p. 118—119° (yield, almost quantitative) (Found: C, 68·9; H, 8·1. Calc. for $C_{24}H_{34}O_6$: C, 68·9; H, 8·1%).

Catalytic Hydrogenation of Andrographolide with Platinum in Acetic Acid.—A solution of andrographolide (0·5 g.) in glacial acetic acid (25 c.c.) was shaken in an atmosphere of pure hydrogen with Adams's platinum oxide (50 mg.). Three mols. of hydrogen were smoothly absorbed in 10—15 minutes; absorption then ceased. The mixture was filtered and the filtrate kept in an evacuated desiccator over potassium hydroxide till four-fifths of the acetic acid was removed. The residual liquid was carefully diluted with water till just turbid. Colourless crystals slowly separated. On recrystallisation from dilute acetic acid these had m. p. 175°. They were dissolved in excess of acetic acid and the solution was diluted with water till just turbid. When this mixture was kept in the ice-chest for 2 days a small quantity of crystals separated, having m. p. 193°. Recrystallised twice from absolute ethanol (ice-chest) they gave glistening plates of the pure high-melting *deoxytetrahydroandrographolide*, m. p. 217° (Found: C, 70·7; H, 10·0. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·0%).

The filtrate obtained after separation of the crystals, m. p. 193°, yielded a second crop when kept in the cold. After several crystallisations from ethanol containing a little water the lower-melting *deoxytetrahydroandrographolide* separated as microscopic needles, m. p. 141° (Found: C, 70·6; H, 9·8%).

Catalytic Hydrogenation of Andrographolide in Methanol in Presence of Palladium.—Andrographolide (0·4 g.) in methanol (40 c.c.) was shaken in an atmosphere of pure hydrogen in presence of 1% palladium chloride solution (2 c.c.) containing some free hydrochloric acid. The shaking was continued for about ½ hour after absorption was complete. After filtration the solution was concentrated under reduced pressure at room temperature until crystals separated. It was then left in the ice-chest overnight. The crystals, m. p. 205°, were then collected and recrystallised several times from absolute ethanol, giving the higher-melting deoxytetrahydroandrographolide as colourless glistening plates, m. p. 217° (Found: C, 70·7; H, 9·9. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·0%).

The filtrate from the crystals of m. p. 205° was treated with water till turbid and left in the ice-chest, giving a second crop of crystals (m. p. 175°). These, after several crystallisations from ethanol, gave more of the higher-melting isomer and, from the mother-liquor, the lower-melting *isomer* which, crystallised from dilute ethanol, had m. p. 141° (Found: C, 70·8; H, 9·8%).

Diacetyldeoxytetrahydroandrographolides.—A solution of diacetyldeoxyandrographolide (0·3 g.) in glacial acetic acid (15 c.c.) was shaken in an atmosphere of pure hydrogen in presence of Adams's platinum oxide (30 mg.). Absorption (2 mols.) was complete in 10 minutes. After separation from the catalyst the clear solution was diluted with water till turbid. Minute crystals slowly separated which were collected and had m. p. 118° (shrinkage at 80—85°). After several crystallisations from ethanol containing a little water the higher-melting *diacetyldeoxytetrahydroandrographolide* was obtained in colourless prisms, m. p. 126° (opaque liquid) (Found: C, 68·3; H, 9·0. $C_{24}H_{38}O_6$ requires C, 68·2; H, 9·0%).

The acid filtrate obtained after separation of the product of m. p. 118° was diluted with an equal volume of water; a second crop of crystals separated. It was collected and after several crystallisations from aqueous ethanol gave the lower-melting *isomer* as silky needles, m. p. 98° (Found: C, 68·0; H, 9·0%).

Hydrolysis of Diacetyldeoxytetrahydroandrographolide, m. p. 126°.—Diacetyltetrahydrodeoxyandrographolide (50 mg.) of m. p. 126° was hydrolysed by a boiling solution of potassium

hydroxide (0·5 g. in water 1 c.c.) and ethanol (10 c.c.) for 1½ hours. Excess of ethanol was evaporated off and the residue was diluted with water. The solution was neutralised with dilute hydrochloric acid and the hydroxy-acid which separated was brought into solution by heat. The hot solution was treated with a few drops of concentrated hydrochloric acid. Minute needle-shaped crystals slowly separated in the cold. Crystallised from ethanol containing a little water, these had m. p. 141° alone or mixed with the lower-melting deoxytetrahydroandrographolide (Found : C, 70·9; H, 10·0%).

Hydrolysis of Diacetyldeoxytetrahydroandrographolide, m. p. 98°.—Hydrolysis of the lower-melting diacetyldeoxytetrahydroandrographolide (50 mg.) was carried out as in the preceding experiment. The product obtained on acidification and lactonisation was crystallised from ethanol, giving shining plates of the deoxytetrahydroandrographolide, m. p. and mixed m. p. 217° (Found : C, 70·8; H, 9·9%).

Catalytic Hydrogenation of Triacetylandrographolide.—Triacetylandrographolide (0·2 g.) in glacial acetic acid (10 c.c.) was shaken in an atmosphere of pure hydrogen in presence of platinum oxide (20 mg.). The absorption (3 mols.) was complete in 10—15 minutes. As the hydrogenated product was difficult to isolate it was directly deacetylated as in the previous experiment. The product obtained in this way had m. p. 175° (Found : C, 70·6; H, 9·7%) and appeared to be a mixture of the two isomers of deoxytetrahydroandrographolides. It did not give a red colour with potassium hydroxide in methanol. The isomers were not separated.

Deoxytetrahydroandrographolic Acid.—The mixed isomers of deoxytetrahydroandrographolide (m. p. 175°) (0·1 g.) obtained above were heated under reflux for an hour with ethanol (1·5 c.c.), water (0·5 c.c.), and potassium hydroxide (0·2 g.). The solution was then treated with some more ethanol and a small amount of charcoal, heated for a short while, and filtered. After removal of excess of ethanol the product was diluted with water, cooled in ice, and acidified to Congo-red with very dilute hydrochloric acid. A flocculent precipitate separated which was immediately filtered off and washed well with ice-cold water. *Deoxytetrahydroandrographolic acid* obtained in this way crystallised from water in silky needles, m. p. 107—108°. It was dried at room temperature *in vacuo* (Found : C, 65·9; H, 10·1. $C_{20}H_{36}O_5,\frac{1}{2}H_2O$ requires C, 65·7; H, 10·1%).

Ozonolysis of Andrographolide.—Ozonised air was passed for 45 minutes through a solution of andrographolide (0·2 g.) in glacial acetic acid (10 c.c.). The product was diluted with an equal volume of water and distilled in steam. The distillate was collected directly in a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-sulphuric acid. The 2 : 4-dinitrophenylhydrazone (0·12 g.) obtained was crystallised from ethanol, separating in yellow silky needles, m. p. 166° alone or mixed with that of formaldehyde.

The solution remaining after steam-distillation was treated with a solution of 2 : 4-dinitrophenylhydrazine in 2N-sulphuric acid. An orange-yellow precipitate was obtained. This was dissolved in ethanol and the solution allowed to crystallise. An extremely small amount of a red crystalline product, m. p. 248° (decomp.), was obtained.

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Department of Chemistry, Bethune College, Calcutta.
Department of Chemistry, School of Tropical Medicine, Calcutta.

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315. *The Infra-red Spectra of Organo-phosphorus Compounds. Part II.* Esters, Acids, and Amines.*

By L. J. Bellamy and L. Beecher.

Correlations suggested earlier for the P=O, P–O–C(aromatic), and P–O–C(aliphatic) bands have received additional confirmation from studies on a further series of compounds. It has been shown that hydrogen bonding in amino- and organic derivatives of phosphorus acids causes a considerable shift of the P=O absorption towards lower frequency, together with an increase in overall intensity. Additional correlations involving the P–O–Et, P–OH (stretching and deformation modes), P–NH_2, and ionic phosphate groupings have been examined and are discussed.

In Part I* we described the infra-red spectra of a number of organo-phosphorus compounds and suggested correlations for a number of structural units. This work has now been extended by the examination of a further series of compounds, in which the correlations previously established have received confirmation and new correlations have been suggested. Particular attention has been paid to the acid and amino-derivatives in an attempt to resolve some anomalies found in respect of the P–OH and P=O bands in these compounds.

Experimental

The compounds examined are listed in the tables. The majority were prepared in these laboratories by standard methods but a substantial number were a gift from Dr. Clarke of Cambridge University. In all cases the physical constants conform with those given in the literature and the samples are believed to be of reasonably high purity.

All spectra were obtained by using the Perkin–Elmer 21B recording double-beam spectrometer with a rock-salt prism.

The general insolubility of the majority of the acids and amines in common solvents has precluded their examination in solution, and most of them were examined as solid pastes ground in paraffin oil. In all cases in which the material could be obtained in a convenient solvent, however, the solution spectra have also been measured.

Results and Discussion

In discussing the results obtained it is convenient to consider separately the three main groups of esters, amino-derivatives, and acids, and to discuss under each group the correlations which can be made for the various types of linkage.

(a) *Esters.*—This group of materials serves mainly to provide additional confirmation for the correlations put forward in Part I (*loc. cit.*) for the P=O, P–O–C(aromatic), and P–O–C(aliphatic) linkages, but the additional number of compounds available has also made it possible to examine further correlations in this series. Table 1 summarises the findings confirming earlier correlations, and includes also the acids, anilides, and amines except as regards the P=O link which will be discussed separately in each case. It will be seen that in all cases bands are found in the expected positions as given in Part I (*loc. cit.*).

As regards further correlations, Daash and Smith (*Analyt. Chem.*, 1951, **23**, 853) have pointed out that the P–O–Et linkage gives rise to absorption almost exactly at 1160 $cm.^{-1}$. We have confirmed this but have noticed also that aromatic phosphates absorb at this point. Altogether 64 organo-phosphorus compounds have been examined, in addition to the salts of the acids, and it is significant that a band in the narrow range 1156—1163 $cm.^{-1}$ is shown by all those in which the P–O–Ph or the P–O–Et group is present. The only exception is ethyl dichlorophosphinite in which the band is at 1143 $cm.^{-1}$. With heavy substituents present in the aromatic ring, the band appears to shift to lower frequencies. In none of the other substances does this particular band appear. Studies of solutions of

* Part I, *J.*, 1952, 475.

comparable concentrations in the same cell also indicate very clearly that there is a correlation between the intensity of this band and the number of either of these groupings in the molecule. On passing through the series triphenyl phosphate, diphenyl chlorophosphonate, and phenyl dichlorophosphinate, for example, there is a progressive weakening in the

TABLE 1. *Confirmation of previous correlations.**

Compound	P=O	P–O–C (Aromatic)	P–O–C (Aliphatic)	P–O–Et or P–O–Ar	P–H
Dibenzyl phosphite	1256	—	1020	—	2410
Di-(1 : 2 : 2-trimethylpropyl) phosphite	1258	—	1020	—	2410
Di*neo*pentyl phosphite	1250	—	1026	—	2381
Di*iso*butyl *p*-(2-ethylhexyl)phenyl phosphate	1279	1215	1020	1174	—
Diethyl ,, ,, ,,	1272	1218	1031	1174—1163	—
Ethyl dichlorophosphinite	—	—	1020	1143	—
Tri-(2-ethylhexyl) phosphate	1282, 1266	—	1031	—	—
Ethyl di-(2-ethylhexyl) phosphate	1250	—	1026	1156	—
Diethyl 2-ethylhexyl phosphate	1250	—	1026	1156	—
Tri-*p*-nitrobenzyl phosphate	1287, 1269	—	1047, 1034	—	—
Tetrabenzyl pyrophosphate	1290	—	1026	—	—
Diphenyl anilinophosphonate	See Table 2	1172	—	1163, 1153	—
Phenyl dianilinophosphinate	See Table 2	1190	—	1163	—
Dibenzyl anilinophosphonate	See Table 2	—	1026	—	—
Dibenzyl benzylaminophosphonate	See Table 2	—	1015	—	—
Dibenzyl *N*-methylanilinophosphonate	1274	—	1026	—	—
Dibenzyl 2-phenylethylaminophosphonate	See Table 2	—	1042	—	—
Dibenzyl morpholinophosphonate	1250	—	1037	—	—
Diphenyl aminophosphonate	See Table 3	1190	—	1163	—
Dibenzyl aminophosphonate	See Table 3	—	1036, 1020	—	—
Phenyl diaminophosphinate	See Table 3	1220	—	1159	—
Diphenyl hydrogen phosphate	See Table 3	1215	—	1156	—
Phenyl dihydrogen phosphate	See Table 3	1183	—	1159	—
Dibenzyl hydrogen phosphate	See Table 3	—	1036	—	—
Di-2 : 4 : 6-trichlorophenyl hydrogen phosphate	See Table 3	1235	—	1130	—
Phenyl hydrogen anilinophosphonate	See Table 3	1183	—	1156	—
Di-*p*-nitrophenyl hydrogen phosphate	See Table 3	1190	—	1147	—
Di-*o*-methoxyphenyl hydrogen phosphate	See Table 3	1190	—	1163	—
Benzyl hydrogen aminophosphonate	See Table 3	—	1026	—	—

* This table omits additional bands in the appropriate regions which we can attribute with reasonable certainty to other causes. Thus a number of the benzylanilino-derivatives absorb at 1220 cm.$^{-1}$ in the P–O–C(Aromatic) region but this is omitted as we shall show later that this is due to the bonded P=O group.

intensity of this band, and the same effect can be observed in the corresponding ethyl esters. This band is relatively more intense with P–O–C(aromatic) substitution than with P–O–Et, giving a strong band in the first case and a medium to weak one in the second. Most of the benzyl and anilino-derivatives give a very weak inflection near 1160 cm.$^{-1}$, which is probably due to the benzene ring itself, but this is so weak that it is not likely to be confused with the P–O–Et or P–O–C(aromatic) band. Presumably this vibration is connected with some mode of the P–O–Et link in the one case, and with an aromatic ring vibration enhanced in intensity by association with the phosphate ester in the other case.

(b) *Amino-derivatives of Phosphorus Acids.*—(1) N–H *Stretching vibration.* It will be seen from Table 2 that the primary and secondary amino-compounds examined exhibit considerable hydrogen bonding in the solid state, as shown by the occurrence of the N–H stretching vibration between 3125 and 3333 cm.$^{-1}$. In several cases two, and even three, bands appear in this region and we would attribute this to different types of hydrogen bonding. Thus the secondary amino-compounds show two peaks in this region when more than one amino-group is present, and this probably arises from the fact that in one group hydrogen is more strongly bonded than in the other. In solution the bonding is broken or much reduced in all these cases and a new band appears in the 3390-cm.$^{-1}$ region.

With the primary amino-compounds three peaks are shown in some cases which

presumably arise from free NH, inter-molecularly bonded NH, and intra-molecularly bonded NH. Some support for this is provided by the persistence of a band (of diphenyl aminophosphonate) in the bonded NH region in solution.

TABLE 2. *Primary, secondary, and tertiary amino-derivatives of phosphorus.*

Compound	N–H (stretching)	NH–C(Ar) (stretching)	P–NH_2 (deformation)	P=O
Diphenyl anilinophosphonate, solid	3125	1290	Nil	1220
,, ,, 5% soln. in $CHBr_3$	3333, 3125, 3520	1290	,,	1290,* 1227
Phenyl dianilinophosphinate, solid	3125, 3333	1277	,,	1220
,, ,, 5% soln. in $CHBr_3$	3378	1290	,,	1290 *
Trianilinophosphine oxide, solid	3125—3333	1279	,,	1214
,, ,, 1% soln. in $CHBr_3$	3367	1274	,,	1290
Dianilinochlorophosphine oxide, solid	3125	1290	,,	1198
Dibenzyl anilinophosphonate, solid	3125	1282	,,	1212
,, ,, 4% soln. in $CHBr_3$	3125—3378	1290	,,	1290,* 1250
Dibenzyl benzylaminophosphonate, solid	3175	Nil	,,	1220—1235
,, ,, 4% soln. in $CHBr_3$	3378	,,	,,	1290
Dibenzyl *N*-methylanilinophosphonate	Nil	,,	,,	1274
Dibenzyl 2-phenylethylaminophosphonate, solid	1325	,,	,,	1212
,, ,, 4% soln. in $CHBr_3$	3390	,,	,,	1290
Dibenzyl morpholinophosphonate	Nil	,,	,,	1250
Trianilinophosphine sulphide	3125—3333	1274	,,	Nil
Diphenyl aminophosphonate, solid	3226, 3436	Nil	1543	1250
,, ,, 2% soln. in CH_3·CN	3300 (solvent)	,,	1580	1274
Dibenzyl aminophosphonate	3125, 3257, 3333	,,	1565	1220
Phenyl diaminophosphinate	3096, 3195, 3333	,,	1558	1176
Phenyl hydrogen anilinophosphonate	3205	1295	Nil	1205
Silver phenyl anilinophosphonate	3175	1290	,,	Nil
Dianilinophosphinic acid	3289	1282	,,	1220
Silver dianilinophosphinate	3125, 3367	1282	,,	Nil
Benzyl hydrogen aminophosphonate	Nil	Nil	,,	1190

* Intensity increase over –NH–C(Ar) stretching intensity. As explained in the text it is not possible to differentiate NH–C(Ar) stretchings and P=O variations near 1300 cm.$^{-1}$, as bromoform has some absorption in this region. A very marked diminution of the band near 1220 cm.$^{-1}$ and an increase at 1290 cm.$^{-1}$ are taken as evidence for breaking of hydrogen bonds on solution. However, this is supported by similar shifts in other compounds in which the anilino-group is absent.

(2) R·NH_2 *Bending*. The three primary amino-compounds examined show a band in the range 1543—1565 cm.$^{-1}$ which is slightly above the normal C–NH_2 bending region. This is probably also associated with hydrogen-bonding effects, for in solution there is a shift to 1580 cm.$^{-1}$ with diphenyl aminophosphonate. Benzyl hydrogen aminophosphonate exhibits no band in this region but there is strong evidence that this exists in the zwitterion form $^-$O·P·NH_3^+ (Clarke and Todd, *J.*, 1950, 2030).

(3) P=O. Examination of the spectra of the series of amino-derivatives given in Table 2 shows that none of the primary amines absorbs strongly in the normal 1250—1300-cm.$^{-1}$ region which we have earlier associated with the P=O link. On the other hand, a strong band appears in the 1175—1250-cm.$^{-1}$ region which is additional to any band arising from the P–O–C(aromatic) linkage. Two of the secondary amines behave similarly, and the remainder show absorption both near 1280 cm.$^{-1}$ and at 1175—1250 cm.$^{-1}$. The tertiary amines appear to be normal in having a P=O absorption between 1250 and 1280 cm.$^{-1}$. Colthup (*J. Opt. Soc. Amer.*, 1950, **40**, 397) has shown that secondary aromatic amines give a band of medium to strong intensity about 1280 cm.$^{-1}$, and we have confirmed this in a number of diphenylamines and related compounds. It is therefore probable that in the secondary amino-compounds the 1250—1280-cm.$^{-1}$ vibration is related to the Ph–NH link, and that in all these compounds, except the tertiary bases, the P=O vibration occurs between 1175 and 1250 cm.$^{-1}$. Confirmation of this has been obtained from studies of solution and salts. It will be seen from Table 2 that on dissolution in bromoform the primary and secondary amines show marked changes in the 1175—1300-cm.$^{-1}$ region. In general, the band between 1175 and 1250 cm.$^{-1}$ which we ascribe to bonded P=O is markedly less intense, whilst the 1300-cm.$^{-1}$ band is stronger. At the same time, any other

band in the 1190—1220-cm.$^{-1}$ region due to the presence of the P–O–C(Ph) group remains unaffected. The increase in intensity of the 1300-cm.$^{-1}$ band is partly obscured by a small absorption due to bromoform in this region, but the enhancement is nevertheless well marked, especially in those compounds in which there is no Ph–NH absorption in this region. These changes are coupled with a corresponding shift of the NH stretching bands in the 3330-cm.$^{-1}$ region which revert to the 3380-cm.$^{-1}$ position corresponding to unbonded NH. In the case of diphenyl aminophosphonate there is evidence of some continued bonding in solution, since the band at 1250 cm.$^{-1}$ does not disappear entirely, and some NH bonding also continues to appear in the 3330-cm.$^{-1}$ region. Nevertheless, the strength of the 1274-cm.$^{-1}$ band in solution indicates that the extent of this association is probably quite small.

Further evidence for the assignment of the bonded P=O absorption to the 1175—1250-cm.$^{-1}$ region is obtained from the comparison of the spectra of the silver salts of dianilinophosphinic acid and *P*-anilino-*P*-phenylphosphinic acid with those of the acids themselves. In the former case the P=O absorption would be expected to vanish and be replaced by the bands of ionic phosphate $\overset{+}{\text{P}}\!<\!\overset{\text{O}^-}{\underset{\text{O}^-}{}}$, and it will be seen that in both cases the 1205—1220-cm.$^{-1}$ band present in the acids is absent from the salts, whereas the 1300-cm.$^{-1}$ Ar–NH band remains substantially unaffected.

This assignment is also supported by the absence of any strong band in the 1175—1250-cm.$^{-1}$ region in aliphatic-type tertiary amines in which hydrogen bonding to the NH is precluded. In these compounds the P=O absorption occurs in the expected region, 1250—1300 cm.$^{-1}$.

Organic Acids and Esters of Phosphorus.—A number of acids of various types have been examined. In most cases their insolubility in organic solvents has necessitated their examination in the solid state, but a few were also examined in solution. The spectra of the silver salts of the majority of these acids have also been obtained for comparative purposes.

(1) *The* P–OH *stretching vibration.* Daash and Smith (*loc. cit.*) have examined several acids of this type and report that in no case could any free hydroxyl be detected in the 3620-cm.$^{-1}$ region. Instead, a broad band appears at about 2680 cm.$^{-1}$ which they attributed to the bonded hydroxyl absorption. It will be seen from Table 3 that our findings confirm this observation and that, in the series of acids we have examined, a shallow, broad band appears near 2560—2700 cm.$^{-1}$ in all cases. In solution in non-polar solvents this band persists and there is no evidence of any free hydroxyl-group absorption. This assignment is considerably beyond the region in which bonded hydroxyl groups normally appear, but exceptional cases of very strong bonding are known in which the OH absorption appears in this region. Thus, Rasmussen, Tunnicliffe, and Brattain (*J. Amer. Chem. Soc.*, 1949, **71**, 1070) find bonded-hydroxyl absorption in the 2700-cm.$^{-1}$ region in β-diketones showing conjugate chelation, and Reid and Ruby (*ibid.*, 1951, **73**, 1054) find that in five substituted tetronic acids the O–H stretching band appears near 2500 cm.$^{-1}$. Further support for this assignment is provided by the disappearance of this band from the spectrum of the silver salts of the corresponding acids.

(2) *The* P–OH *deformation vibration.* The O–H deformation vibration is normally subject to considerable influences from the surrounding structure and is therefore liable to show marked shifts in position with alteration in the nature of adjacent groups. However, on general grounds, it would be expected to appear in the 1050-cm.$^{-1}$ region of the spectrum. In the case of acids containing P–O–C(aliphatic) linkages, this region of the spectrum is obscured by the strong phosphorus–ether-link absorption, but with all the other acids it will be seen that there is a strong band in the 1000—1040-cm.$^{-1}$ region. Furthermore, this band vanishes on conversion of the acid into the silver salt, a new band appearing near 1075 cm.$^{-1}$ which, as will be seen later, we attribute to an ionic-phosphate vibration.

There is also support for this assignment from the comparison of the spectra of the acids with three of the corresponding fully substituted esters. Triphenyl phosphate, for example, shows no absorption in the 1030-cm.$^{-1}$ region although this is present in both the mono- and the di-phenyl hydrogen phosphates. We would therefore assign the P–OH deformation mode to the 1030-cm.$^{-1}$ region at least insofar as the present range of materials is concerned.

(3) P=O *in acids.* In view of the results already obtained with amino-derivatives of phosphorus, and the fact that there is evidence of abnormally strong hydrogen bonding from the O–H stretching region, it is to be expected that the P=O absorption will be shifted into the 1175—1250-cm.$^{-1}$ region. This has been found to be the case, and in only one of the acids examined has the frequency risen above 1250 cm.$^{-1}$. This is di-*o*-methoxyphenyl hydrogen phosphate (P=O, 1261 cm.$^{-1}$), in which there is the possibility of a steric effect similar to the well-known *ortho*-effect in methoxyphenols which would reduce to some extent the tendency towards strong hydrogen-bond formation on the P=O group. The frequency shifts observed in the P=O absorption are in line with those reported by Daash and Smith (*loc. cit.*) for a number of other acids of phosphorus.

TABLE 3. *Acids and salts of phosphorus.*

Compound	P–OH (stretching)	1600—2500-cm.$^{-1}$ region	P=O	P–OH (deformation)	$P\langle^{O-}_{O-}$	(ionic)	P–O– (970 cm.$^{-1}$)
Diphenyl hydrogen phosphate, anhydr., solid	2597 broad	1667 & 2000—2275	1250	1026	—	926 (w)	952
Diphenyl hydrogen phosphate, anhydr., soln. in CS_2 and CCl_4	as dry solid throughout						
Diphenyl hydrogen phosphate, anhydr., soln. in NEt_3	2597	1626 & 2470 both sharp	1242	Solvent	Solvent	885 & 909	Nil
Diphenyl hydrogen phosphate, anhydr., soln. in NEt_2Ph	2632	2381 (Solvent)	Solvent	Solvent	Solvent	885 & 909	Nil
Diphenyl hydrogen phosphate, anhydr., soln. in C_5H_5N	2564	1626, 2000, 2105, 2410	1250 (broad)	Solvent	Solvent	885 & 909	Nil
Diphenyl hydrogen phosphate dihydrate, solid	2667 broad	1709 & 2222	1212	—	1058	935 (s), 922 (s)	Nil
Silver diphenyl phosphate	Nil	Nil	Nil	Nil	1075	930	Nil
Phenyl dihydrogen phosphate, hydrate	2667 (shoulder)	2222 only	1220	1036	1087?	917	980 (w)
Phenyl dihydrogen phosphate, soln. in trioctyl phosphate	2597 (s)	2273 only	not measured				
Disilver phenyl phosphate	Nil	Nil	Nil	1034	1042?	1080, 917 (m)	985
Dibenzyl hydrogen phosphate	2564	1695, 2128, 2273	1250	P–O–C absorption	Nil	Nil	985'(s)
Silver dibenzyl phosphate	Nil	Nil	Nil	P–O–C absorption	1081	917 (m)	990 (m)
Di-2 : 4 : 6-trichlorophenyl hydrogen phosphate	2703	1709, 1942, 2174, 2353	1220	1015	Nil	Nil	957 (s)
Silver di-2 : 4 : 6-trichlorophenyl phosphate	Nil	Nil	Nil	Nil	1075, 1087	901 (s), 909	Nil
Phenyl hydrogen anilinophosphonate	2564	1695, 2273	1205	1010 (v.s.)	Nil	Nil	975 (v.s.)
Silver phenyl anilinophosphonate	Nil	Nil	Nil	Nil	1053	926 (v.s.)	Nil
Dianilinophosphinic acid	2667	1639, 2273, 2381	1220	1015	1031?	Nil	952
Silver dianilinophosphinate	Nil	Nil	Nil	Nil	1042 (s)	901 (w), 930	Nil
*cyclo*Hexylphosphonic acid	2667	2273 only	1220	1000?	Nil	Nil	952
Di-*p*-nitrophenyl hydrogen phosphate	2632	1667, 1923, 2353	1220	1010	Nil	935 (m)	980 (v.s.)
Di-*o*-methoxyphenyl hydrogen phosphate	2632	1639, 2000	1261	1026	Nil	909 (m)	975 (v.s.)
Benzyl hydrogen aminophosphonate	w. shoulder only	1695, 1852, 2326	1190?	Nil (P–O–C)	1053	Nil	952

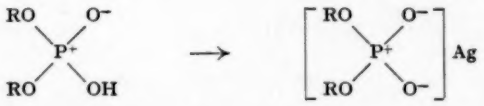
In the above analysis, a strong band occurring in the 1190—1220-cm.$^{-1}$ region in the silver salts of aromatic acids has been ascribed to the P–O–C(Ar) link and in the absence of other bands the P=O has been marked absent.

In the case of the aromatic acids there is also a band in the 1190—1220-cm.$^{-1}$ region arising from the P–O–C(Ph) link and in some cases this coincides with the P=O absorption. The influence of the P=O absorption is, however, clearly shown on comparison with the spectra of the silver salts. In the latter case only the P–O–C(aromatic) band appears as a sharp peak clearly distinguishable from the broad band obtained when the P=O group is also present.

A number of the acids examined appear to exist as hydrates from which the water could only be removed with extreme difficulty. When this was done there appeared to be some resulting shift in the P=O absorption towards higher frequencies. Thus diphenyl hydrogen phosphate absorbs at 1250 cm.$^{-1}$ in the dry state and at 1212 cm.$^{-1}$ as the hydrate.

The frequency shift accompanying hydrogen bonding of the P=O group in both the acid and the amino-series appears to be associated with a very marked increase in the intensity. The shifts themselves are also very much greater than would be expected to result from normal hydrogen bonding. Thus normal hydrogen bonding of carbonyl linkages rarely results in shifts of more than 10—20 cm.$^{-1}$ (Rasmussen *et al.*, *loc. cit.*) and this order of shift is also shown by bonded sulphoxides (Barnard, Fabian, and Koch, *J.*, 1949, 2442). On the other hand, conjugated chelated β-diketones and some related unsaturated β-hydroxy-ketones show very considerable C=O shifts (Rasmussen *et al.*, *loc. cit.*) accompanied by considerable intensity increases. This effect is associated with the appearance of the O–H stretching absorption at 2700 cm.$^{-1}$, at which point the O–H absorption is also found in our acid phosphates. Presumably, therefore, the organic derivatives of phosphoric acids and amides exist in a bonded form in which the strength of the bonds is comparable with those of these chelated products.

(4) *The ionic-phosphate vibration.* Salt formation with the organic acids of phosphorus would be expected to result in a considerable weakening of the P=O band, with consequent shift to lower frequencies. This would arise from the introduction of a second negatively charged oxygen atom so that the P=O group would become effectively the ionic phosphate group :



An analogous effect is well known with salts of carboxylic acids. This expectation is borne out in practice, and in all cases, the bands ascribed to the P=O vibration and to the P–OH deformation in the free acid disappear in the silver salts and are replaced by a single absorption band in the 1050—1110-cm.$^{-1}$ region. This is the region which Colthup (*loc. cit.*) has associated with the ionic-phosphate vibration and we would therefore assign it to that cause. It is noteworthy that certain of the hydrated compounds also show some evidence of a band in this region and it may be that they also tend to exist, in part, in the ionic form in the solid state. There is evidence of a second band near 900 cm.$^{-1}$ which may also be associated with the ionic phosphate group (see Table 3).

(5) *The* 1660—2500-*cm.*$^{-1}$ *band.* All the acids examined show broad shallow bands in this region which recall those arising from amino-acids and zwitterion substances. However, only the monobasic acids exhibit a broad band in the region of 1665 cm.$^{-1}$, and possibly when a sufficient number of acids have been examined this may be of value in differentiating mono- and di-basic organic derivations of phosphoric acids.

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ROYAL ARSENAL, WOOLWICH. [*Received, November 28th*, 1951.]

316. *Kinetics of the Interaction of Hydrogen Chloride with Styrene in Presence of Stannic Chloride.*

By Gwyn Williams and (Mrs.) Hetty Bardsley.

At low concentrations of styrene (~0·1M) and catalyst, the rate of consumption of styrene by hydrogen chloride (to form mainly 1-phenylethyl chloride), in carbon tetrachloride medium, is proportional to the concentration of catalyst and of each reagent. With M-styrene the rate becomes independent of styrene concentration. The facts are consistent with a carbonium ion mechanism, but they do not decide whether initiation is by interaction of catalyst with hydrogen chloride or with styrene.

In carbon tetrachloride solution, in the presence of stannic chloride, styrene reacts with hydrogen chloride to form 1-phenylethyl chloride and short-chain polystyrenes, mainly the dimer to the tetramer (Williams, *J.*, 1938, 1046; Williams and Thomas, *J.*, 1948, 1867). The amounts, and the molecular weights, of the polymers found in the reaction products increase with rising initial concentration of styrene. With 0·08—0·17M-styrene, 75% of the initial material is recovered as 1-phenylethyl chloride. This paper describes experiments on the kinetics of the reaction.

The rate of the reaction is measured by following the fall of styrene concentration with time. This has to be done because of the difficulty of estimating hydrogen chloride in the presence of stannic chloride; but it has the drawback that some styrene is known to be consumed in short-chain polymerisation as well as in forming the addition product. However, with low reagent concentrations, and with hydrogen chloride present in excess over styrene, some simple kinetic relations are discernible.

In the following, a, b, and c are the initial concentrations of hydrogen chloride, styrene, and stannic chloride, respectively, in moles per litre. Time is in minutes.

In carbon tetrachloride, there is no reaction in the absence of the catalyst (see Table 5).

The Influence of Styrene Concentration.—The effects of changing styrene and stannic chloride concentrations on the rate of reaction between styrene and hydrogen chloride

Table 1. *Influence of styrene concentration. Temp.* 25°.

$SnCl_4$ concn., M.	Expt. no.	HCl concn., M.	Styrene concn., M.	k_1	$k = k_1/ca$
0·0109	46	0·143	0·0335	0·0093	6·0
	45	0·143	0·0365	0·0095	6·1
	47	0·146	0·185	0·0097	6·1
	48	0·146	0·185	0·0096	6·0
0·0125	28	0·143	0·0324	0·0130	7·3
	29	0·145	0·136	0·0125	6·9
	32	0·145	0·146	0·0125	6·9
0·0126	38	0·146	0·178	0·0133	7·2
	42	0·151	0·395	0·0146	7·7
0·0152	25	0·144	0·0386	0·0154	7·0
	22	0·145	0·133	0·0157	7·1
	24	0·145	0·152	0·0162	7·4
0·0156	19	0·144	0·0486	0·0146	6·5
	18	0·145	0·102	0·0151	6·7
	20	0·145	0·136	0·0151	6·7
	21	0·145	0·137	0·0156	7·4
0·0224 *	149	0·276	0·030	0·0102	1·65
	152	0·276	0·101	0·0098	1·59

* At 0°.

have been investigated with solutions containing hydrogen chloride at its constant saturation concentrations in the carbon tetrachloride medium. This condition was ensured by passing a stream of dry hydrogen chloride through the carbon tetrachloride solution of styrene and stannic chloride while the reaction was proceeding, the fall of

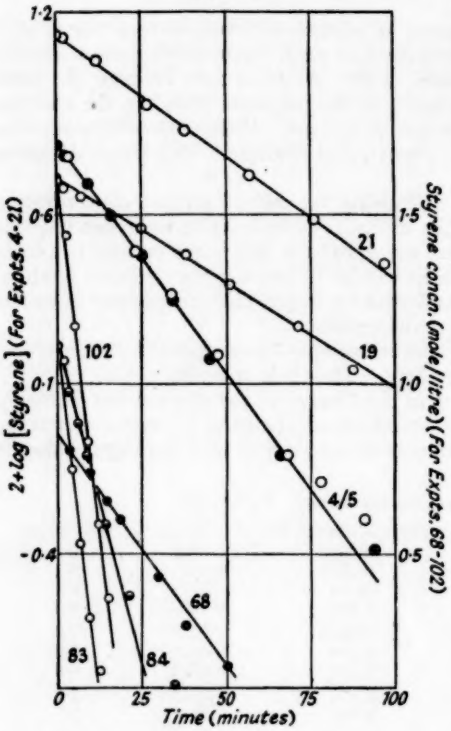
styrene concentration with time being measured. In these circumstances, at a fixed concentration of catalyst, the rate of reaction is given by equation (1), for 0·03—0·2M initial styrene concentration :

$$-d[C_8H_8]/dt = k_1[C_8H_8] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Log $[C_8H_8]$ is linear with time in individual experiments (Fig. 1; the divergent points in expts. 4/5 are for conversions of 90% and more); and the coefficient k_1 is independent of the initial styrene concentration (Table 1).

The variations of hydrogen chloride concentration in Table 1 arise from the varying solubility of the gas in solutions of different styrene concentrations (see Table 4). These variations are automatically corrected in the last column of Table 1.

FIG. 1.



The Influence of Stannic Chloride Concentration.—This was also studied, with a flow system, at constant concentration of hydrogen chloride. The results are shown in Table 2.

At 25° the velocity coefficient k_1 of equation (1) is approximately proportional to the catalyst concentration over the range 0—0·016M-$SnCl_4$ (see Fig. 2). With higher catalyst concentrations, the rate of reaction increases less than proportionally to the stannic chloride concentration. At 0°, there is little departure from a linear relation up to 0·038M-concentration of stannic chloride.

The Influence of Hydrogen Chloride Concentration.—In order to vary the initial concentration of hydrogen chloride, the use of saturated hydrogen chloride solutions must necessarily be abandoned. It has proved to be very difficult to prepare reliable hydrogen chloride solutions in carbon tetrachloride at other concentrations, because of the extreme volatility of the hydrogen chloride. Table 3 shows the results of experiments made with a closed reaction system (see Experimental section). In this Table, the velocity coefficients, k_2, are calculated from the equation :

$$-d[C_8H_8]/dt = k_2[C_8H_8][HCl] \quad . \quad (2)$$

Each value for k_2 is the mean of several observations, made at different times, upon independently prepared reaction mixtures. The reproducibility is only moderate (see Experimental section).

The results of Table 3 justify the conclusion that equation (2) is valid up to the saturation concentrations of hydrogen chloride at 25° and at 0°. The best demonstration is contained in Fig. 2, which shows that, when plotted against catalyst concentration, the "static" values of k_2 (full black circles) from Table 3 fall nearly on the same curves, at the two temperatures, as the values of $k_1/[HCl]$ derived from Tables 1 and 2 for experiments with the flowing stream of hydrogen chloride.

In similar experiments in a closed system, but with the initial concentration of styrene greater than that of hydrogen chloride, k_2 rose with time (indicating transition to a lower reaction order) and the styrene concentration fell below the value corresponding to the formation of 1-phenylethyl chloride alone. No doubt some distyrene was formed.

The above results may be summarised by the statement that, at 25°, for $[SnCl_4] \leqslant 0{\cdot}016$M, $[HCl] \leqslant 0{\cdot}15$M (saturation concentration), and for [HCl] > [Styrene], the reaction velocity is given by equation (3):

$$-d[C_8H_8]/dt = k[SnCl_4][C_8H_8][HCl] \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

In equations (1), (2), and (3),

$$k = k_2/c = k_1/ca; \; k_2 = k_1/a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

the symbols being as defined at the beginning of this paper. From Tables 1 and 2, $k = 6{\cdot}9$ at 25° and 1·61 at 0°. At 0°, equation (3) is valid over greater concentration ranges, at least up to $[SnCl_4] = 0{\cdot}038$M and $[HCl] = 0{\cdot}28$M.

The variation in k between 0° and 25° corresponds to an overall activation energy of 9·4 kcal. The overall activation energy for the long-chain polymerisation of styrene

TABLE 2. *Influence of stannic chloride concentration.*

$SnCl_4$ concn., M.	Expt. no.	HCl concn., M.	Styrene concn., M.	k_1	k_1/[HCl]	$k = k_1/ca$
Temp. 25°.						
0·0047	33	0·145	0·0964	0·0062	0·0430	9·2
	36	0·145	0·0858	0·0042	0·0290	6·2
0·0100	86	0·144	0·0442	0·0079	0·0547	5·5
	85	0·144	0·0672	0·0077	0·0535	5·4
0·0109		Average from Table 1		0·0095	0·066	6·1
0·0116	8	0·144	0·0455	0·0124	0·0861	7·4
0·0125		Average from Table 1		0·0127	0·0878	7·0
0·0126		Average from Table 1		0·0140	0·0964	7·5
0·0132	12	0·145	0·127	0·0133	0·0917	7·0
0·0152		Average from Table 1		0·0158	0·109	7·2
0·0154	16	0·143	0·0329	0·0139	0·0972	6·4
	17	0·154	0·0574	0·0152	0·106	6·9
0·0156		Average from Table 1		0·0151	0·106	6·8
0·0226	11	0·145	0·0994	0·0184	0·127	5·6
0·0312	2	0·144	0·0604	0·0225	0·156	5·0
	3	0·144	0·0604	0·0230	0·160	5·1
0·0363	60	0·143	0·0328	0·0255	0·178	4·9
0·0539	10	0·144	0·058	0·0271	0·188	3·5
0·0887	4	0·144	0·0638	0·0317	0·220	2·5
	5	0·144	0·0638	0·0306	0·212	2·5
Temp. 0°.						
0·0100	150	0·276	0·0306	0·00430	0·0156	1·57
0·0122	148	0·276	0·0300	0·00569	0·0206	1·69
0·0224		Average from Table 1		0·0100	0·0362	1·62
0·0384	151	0·276	0·0302	0·0165	0·0598	1·56

TABLE 3. *Influence of hydrogen chloride concentration.*

Expt. no.	$SnCl_4$ concn., M.	Styrene concn., M.	HCl concn., M.	k_2	k_2/c
Temp. 25°.					
140	0·0086	0·0301	0·0712	0·043	4·8
145	0·0111	0·0284	0·0712	0·074	6·7
139	0·0116	0·0301	0·0712	0·065	5·6
138	0·0117	0·0301	0·0712	0·056	4·8
144	0·0105	0·0284	0·0284	(0·104)	6·9
From " flow " expts. at 25°			0·143	—	6·9
Temp. 0°.					
192	0·0179	0·0294	0·0918	0·026	1·5
193	0·0179	0·0294	0·184	0·027	1·5
From " flow " expts. at 0°			0·276	—	1·6

with stannic chloride in carbon tetrachloride medium is about 3 kcal. (Williams, *J.*, 1940, 775). Both of these activation energies are composite.

High Styrene Concentrations.—With the initial styrene concentration ⩾1M, and with streaming hydrogen chloride, kept at constant (saturation) concentration (*ca.* 0·16M), the process (up to at least 60% consumption of styrene) is better described (except at very low concentrations—0·005M—of $SnCl_4$) by the zero-order equation (5) than by equation (1) (see Fig. 1, expts. 68—102).

$$-d[C_8H_8]/dt = k_0; \; ([HCl] \text{ and } [SnCl_4] \text{ const.}) \quad . \quad . \quad . \quad . \quad (5)$$

Since the styrene is largely consumed by the continuous supply of hydrogen chloride, the zero-order behaviour is not to be ascribed purely to the excess of styrene present.

On the assumption that the reaction rate is still proportional to the hydrogen chloride concentration, k_0/[HCl] has been plotted against stannic chloride concentration, in Fig. 3, for experiments with seven different stock preparations of stannic chloride, always with initial concentration in the range 0·85—1·1M. Although the fluctuations are considerable, equation (6) holds approximately for these experimental conditions, up to a much higher concentration of stannic chloride than does equation (3) for low styrene concentrations (cf. Fig. 2).

$$-\mathrm{d}[C_8H_8]/\mathrm{d}t = k''[SnCl_4][HCl];\ (\text{initial } [C_8H_8] \sim 1\text{M}) \quad . \ . \ . \quad (6)$$

In equations (5) and (6), $k'' = k_0/[SnCl_4][HCl]$; and, from Fig. 3, $k'' \sim 5{\cdot}2$. This equation probably has a limited validity, for there is some evidence that k'' rises with initial concentration of styrene above 1M. For example, in one series, $k'' = 4{\cdot}8$ and $9{\cdot}2$

FIG. 2. *Styrene concentration* 0·03—0·1M.

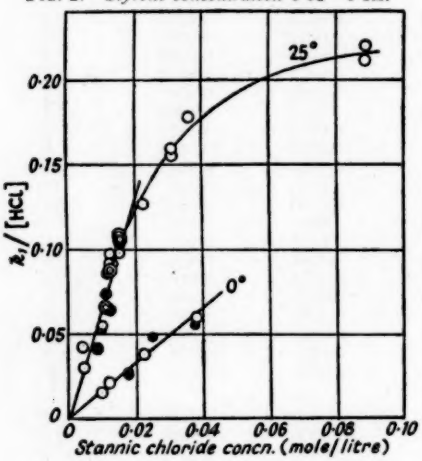
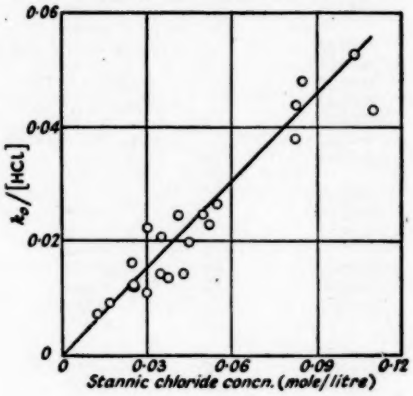


FIG. 3. *Initial styrene concentration* 0·8—1·1M.



for 1·07M and 1·60M initial styrene, respectively. Analogous behaviour has been observed (Williams, 1940, *loc. cit.*) in the long-chain polymerisation of styrene by stannic chloride in carbon tetrachloride, where a third-order velocity coefficient, valid for given initial conditions, rises with increasing initial styrene concentration in the range 0·4—3·5M. If these reactions have a carbonium ion mechanism, it is conceivable that their speeds are influenced by changes in the dielectric constant of the system (cf. Pepper, *Trans. Faraday Soc.*, 1949, **45**, 397, 404; George and Wechsler, *J. Polymer Sci.*, 1951, **6**, 725) occurring when the proportion of styrene to carbon tetrachloride (having a low dielectric constant) is substantially altered, as it is when initial styrene concentrations above 1M are changed. Velocity coefficients are independent of initial styrene concentrations when these are *low* (Table 1).

Fig. 3 and equation (6) have an empirical use for estimating the kinetic chain-length in the long-chain polymerisation of styrene by experiments on the inhibiting action of small concentrations of hydrogen chloride (unpublished results of Mr. J. S. Coe, M.Sc.).

DISCUSSION

To account for the products of reaction, a carbonium ion mechanism has already been suggested (Williams and Thomas, *loc. cit.*), in accordance with the general opinion about the action of Friedel–Crafts catalysts. This mechanism requires co-operation of the three

reactants in processes which have the result shown in equation (7) (the ion $SnCl_6^-$ might also be formed):

$$CHPh{:}CH_2 + SnCl_4 + HCl \longrightarrow {}^+CHPh{\cdot}CH_3\}SnCl_5^- \quad . \quad . \quad . \quad . \quad . \quad (7)$$

In the previous paper, the initial steps were formulated:

$$(\alpha)\ HCl + SnCl_4 \rightleftharpoons H^+\}SnCl_5^-$$

$$(\beta)\ CHPh{:}CH_2 + H^+\}SnCl_5^- = {}^+CHPh{\cdot}CH_3\}SnCl_5^-$$

Here the hydrogen chloride would act as a co-catalyst to the stannic chloride (cf., *e.g.*, Plesch, *Research*, 1949, **2**, 267). An argument for the interaction (α) was Meerwein's observation (*Annalen*, 1927, **453**, 16) that dilute ethereal solutions of hydrogen chloride and of stannic chloride are, separately, yellow after addition of the indicator *p*-dimethylaminoazobenzene; but that an immediate red (acid) colour is formed when the solutions are mixed. We have confirmed this result in ethereal solution, but not in the solvent *carbon tetrachloride*. Meerwein's experiment rested on Hantzsch's observation (*Ber.*, 1925, **58**, 612) that an ethereal solution of hydrogen chloride, coloured red with the indicator, becomes yellow on sufficient dilution with more ether. Hantzsch said that this colour inversion did not occur in the solvent chloroform. It does not occur, either, in carbon tetrachloride. The indicator behaviour in ether may be accounted for by solvation of the proton; and the argument for the occurrence of reaction (α) in carbon tetrachloride, by analogy with Meerwein's result, therefore fails.

On the other hand, the racemisation of 1-phenylethyl chloride by stannic chloride in benzene solution (Bodendorf and Böhme, *Annalen*, 1935, **516**, 1) is greatly retarded by hydrogen chloride (Böhme, *Ber.*, 1938, **71**, 2372); and immobilisation of the stannic chloride catalyst through complex formation with hydrogen chloride has been proposed as the explanation. The explanation would be more satisfactory if there were independent evidence for the complex ($HCl + SnCl_4$) in benzene solution. The reaction (*d*) below will not account for the retardation, because it should assist racemisation.

The pairs of compounds ($AlCl_3 + HCl$) and ($AlBr_3 + HBr$) catalyse the isomerisation of paraffins, in presence of olefin (*e.g.*, Pines and Wackher, *J. Amer. Chem. Soc.*, 1946, **68**, 595; Fontana and Kidder, *ibid.*, 1948, **70**, 3745); and the complex acids $HAlCl_4$ and $HAlBr_4$ have been mentioned as possible intermediates in reactions of this type (Schmerling, *ibid.*, 1944, **66**, 1422; 1945, **67**, 1778; Bloch, Pines, and Schmerling, *ibid.*, 1946, **68**, 153); but physical evidence for their existence in hydrocarbon solvents is lacking (Fontana and Herold, *ibid.*, 1948, **70**, 2881; Schmerling and Ipatieff, *Adv. in Catalysis*, 1950, **2**, 28). Plesch has suggested (*J. Applied Chem.*, 1951, **1**, 269) that interaction of type (α) between hydrogen chloride and stannic chloride is unlikely to occur in a solvent, such as carbon tetrachloride, which cannot readily solvate the proton, and that an alternative is complex formation between stannic chloride and the aromatic ring of styrene.

Another suggestion for the initial step in the reaction of hydrogen chloride with styrene is the reaction pair (*a*) and (*b*):

$$(a)\ CHPh{:}CH_2 + SnCl_4 \rightleftharpoons \overset{+}{C}HPh{\cdot}CH_2{\cdot}\overset{-}{S}nCl_4$$

$$(b)\ \overset{+}{C}HPh{\cdot}CH_2{\cdot}\overset{-}{S}nCl_4 + HCl = \overset{+}{C}HPh{\cdot}CH_3\}SnCl_5^-$$

The kinetic results obtained do not distinguish between the pair ($\alpha + \beta$) and the pair ($a + b$). Among steps which may succeed either pair are:

$$(c)\ \overset{+}{C}HPh{\cdot}CH_3\}SnCl_5^- \rightleftharpoons CHPhCl{\cdot}CH_3 + SnCl_4$$

$$(d)\ HCl + \overset{+}{C}HPh{\cdot}CH_3\}SnCl_5^- = CHPhCl{\cdot}CH_3 + SnCl_4 + HCl$$

$$(e)\ CHPh{:}CH_2 + \overset{+}{C}HPh{\cdot}CH_3\}SnCl_5^- = \overset{+}{C}HPh{\cdot}CH_2{\cdot}CHPh{\cdot}CH_3\}SnCl_5^-$$

$$(f)\ \overset{+}{C}HPh{\cdot}CH_2{\cdot}CHPh{\cdot}CH_3\}SnCl_5^- = CHPh{:}CH{\cdot}CHPh{\cdot}CH_3 + HCl + SnCl_4$$

Further steps (suggested in the previous paper, *loc. cit.*) may form saturated distyrene and higher polymers. Only di- and tri-styrenes are formed in appreciable amount at low styrene concentrations.

The carbonium-ion mechanism and reversibility for (*c*) are made very probable for a number of solvents by Bodendorf and Böhme's demonstration (*loc. cit.*) of the racemisation of optically active 1-phenylethyl chloride by stannic chloride. Racemisation in the solvent carbon tetrachloride has since been proved (unpublished experiments by Mrs. K. Heald, M.Sc.). The reversibility of (*c*) in carbon tetrachloride follows also, first, because 1-phenylethyl chloride reacts with styrene in presence of stannic chloride, to form distyrene (Williams and Thomas, *loc. cit.*), and, secondly, because halogen exchange occurs between $CHPhCl{\cdot}CH_3$ and $SnBr_4$, and between $CHPhBr{\cdot}CH_3$ and $SnCl_4$ (experiments by Mrs. K. Heald). A step such as (*d*) may help to account for a retardation of the halogen exchange by hydrogen halide (but cf. Böhme, *loc. cit.*).

The steps outlined may be combined (with the stationary-state hypothesis) to give a complex kinetic equation which reduces to equation (3) for low reagent concentrations, and contains a term suggesting a qualitative explanation for the transition to equation (6) at high styrene concentrations by increasing intrusion of back-reaction (*c*) and step (*e*) as reaction proceeds. Information about the relative rates of individual steps is needed to test this explanation.

Experimental

Materials.—Styrene was made from 2-phenylethyl alcohol and potassium hydroxide (Sabetay, *Bull. Soc. chim.*, 1929, **45**, 69). Pure commercial styrene, washed with alkali, dried, and re-distilled, was also used. The reaction medium was AnalaR carbon tetrachloride, washed with water, dried (KOH), and distilled. Commercial stannic chloride was purified by repeated distillation, under a high vacuum, in a completely closed, all-glass apparatus (cf. Williams, *J.*, 1938, 246), being collected in a series of sealed glass bulbs. For stannic chloride which was to be used in solutions saturated with hydrogen chloride, a simplified method of purification proved satisfactory. With this method, stannic chloride was distilled in an atmosphere of dry hydrogen chloride at 0·1 mm. in an apparatus partly fitted together with ground joints lubricated by " Silicone " grease. It was again collected in sealed bulbs. It was observed that stannic chloride could be preserved for long periods as a clear solution in carbon tetrachloride containing dissolved hydrogen chloride. In the absence of hydrogen chloride, a turbidity develops gradually. The steady current of hydrogen chloride required for kinetic experiments was generated by running concentrated hydrochloric acid (with a head of 3 ft. to ensure sufficient gas pressure) into concentrated sulphuric acid. The gas passed through sulphuric acid, carbon tetrachloride, and a flow-meter before entering the reaction train.

Analytical Methods.—Styrene, in carbon tetrachloride solution, was determined by quantitative bromination (bromine in glacial acetic acid) (Williams, 1938, *loc. cit.*). Tests with prepared styrene and with commercial styrene gave: 0·1079, 0·1920M. Calc.: 0·1077, 0·1911M. Hydrogen chloride, in carbon tetrachloride solution, was determined either with standard potassium iodate and sodium thiosulphate solutions, or, if styrene was also present, with standard alkali.

The Saturation Concentration of Hydrogen Chloride.—The saturation concentrations of hydrogen chloride in pure carbon tetrachloride and in solutions containing various concentrations of styrene, at 25°, were found to be those given in Table 4. The saturation concentration of hydrogen chloride is linear with the styrene concentration over the range investigated.

Table 4. *Saturation concentration of hydrogen chloride.*

Styrene concn., M:	0	0·1113	0·479	0·979	1·197	1·304	1·622
HCl concn., M.	0·1423	0·1460	0·1516	0·1623	0·1651	0·1693	0·1759

At 0°, the saturation concentration of hydrogen chloride in pure carbon tetrachloride was found to be 0·276M (cf. Table 5).

Reaction Velocities with Streaming Hydrogen Chloride.—A train of glass vessels, *A*, *B*, *C*, *D*, *E* (each of about 100-c.c. capacity) was mounted in a thermostat. A current of dry hydrogen chloride was led through the train, entering each flask at the bottom and leaving at the top. Each vessel had a stoppered outlet for the removal of samples for analysis. The reaction vessel *C* was protected by sealed-on traps to prevent accidental entry of liquid. Initially, *B* contained a standard solution of styrene in carbon tetrachloride; *A* and *E* contained pure solvent. When all solutions were saturated with hydrogen chloride (requiring about 30 minutes), a weighed

bulb of stannic chloride was smashed under carbon tetrachloride from *E*, to form the standard catalyst solution. A known volume of styrene solution from *B* was transferred to *C*, and reaction was started in *C* by addition of a known volume of catalyst solution. Samples were extracted with a pipette at known time intervals, and analysed for styrene. The concentration of stannic chloride was eventually established by filtering and weighing the glass from the smashed bulb in the stock solution.

The result of these operations was to furnish, in the reaction vessel *C*, solutions of styrene and catalyst, both pre-saturated with hydrogen chloride, and to lead through the liquid in *C* a current of hydrogen chloride pre-saturated with the vapour of the solvent. Without the various precautions taken, there were slow changes of concentration of the reagents in *C* when no reaction was taking place. With them, concentrations remained constant, in the absence of catalyst as the figures in Table 5 show.

TABLE 5.

Steady concentration of hydrogen chloride at 25°.

Time (min.)	15	40	50	110	120
HCl, M	0·1126	0·1420	0·1420	0·1420	0·1420

Steady concentration of styrene at 25° in HCl current.

Time (min.)	4	9	15	30	60	65
Styrene, M ...	0·0971	0·0968	0·0968	0·0972	0·0972	0·0975

Steady concentration of hydrogen chloride at 0°.

Time (min.)	21	42	51	58	66
HCl, M	0·2612	0·2755	0·2748	0·2765	0·2755

Steady concentration of styrene at 0° in HCl current.

Time (min.)	4	27	39	45	75	87	99	120
Styrene, M ...	0·0391	0·0385	0·0385	0·0385	0·0384	0·0384	0·0384	0·0384

The bulb *D* in the train was charged with carbon tetrachloride while reaction was in progress in *C*. Analysis of samples from *D* for hydrogen chloride served to check the adequacy of the supply of gas passing through *C*. Separate experiments showed that rate of supply of hydrogen chloride to *C* was (1—5) $\times$ 10^{-4} mole per sec. The maximum consumption of hydrogen chloride did not exceed 3 $\times$ 10^{-5} mole per sec.

Experiments at 0° were carried out with an apparatus similar in principle, but simplified so as to allow the essential portions to fit into a large Dewar vessel containing ice-water.

The first-order velocity coefficients were always evaluated graphically (cf. Fig. 1). The reproducibility may be judged from the results given in Tables 1 and 2 (see also Fig. 1, expts. 4/5).

The figures in Table 5 serve to prove that there is no reaction between styrene and hydrogen chloride at 0° and 25°, in carbon tetrachloride in the absence of the catalyst (cf., also, Williams and Thomas, *loc. cit.*).

Reaction Velocities in Closed System.—Attempts to construct an apparatus, in which a series of samples for analysis could be withdrawn from a reaction mixture containing hydrogen chloride at less than its saturation concentration, failed, owing to losses of hydrogen chloride gas from the solution. Eventually, independent reaction mixtures were made up in 10-c.c. stoppered tubes; and the styrene concentrations in each tube were measured after different times. Loss of hydrogen chloride at the end of the reaction did not matter, since it was the styrene which was determined; but it was essential to prove that the *initial* hydrogen chloride concentration was correctly known. This was done by running in 5 c.c. of a saturated hydrogen chloride solution, in carbon tetrachloride, under the surface of 5 c.c. of the same solvent in a reaction tube sealed through an internal ground joint (which could be stoppered) to an upper tube (also stoppered). After the mixture had been made up, water was placed in the upper tube. In an analysis for hydrogen chloride, the internal stopper was removed to admit water to the carbon tetrachloride solution, and instantly replaced. After being shaken, the mixture was poured into excess of standard alkali. Results were :

Concn. of hydrogen chloride in tube :

Calc. : 0·0712M. Found : 0·0708, 0·0708, 0·0714, 0·0712M.

Reaction mixtures containing catalyst were made up in a similar way, the known volume of saturated hydrogen chloride solution being added last. Velocity coefficients were calculated from equation (2). Owing to the number of operations involved in making up individual

reaction mixtures for each reading, with the risk of loss of gas, the reproducibility of the results was mediocre (Table 3). Expt. 140 is an example.

Expt. 140. *Initial concn.: styrene*, 0·0301M: *hydrogen chloride*, 0·0712M; *stannic chloride*, 0·0086M.

Time (min.)	49·5	86·3	129·8	158·0	109·0	181·3	222·5
Conversion, %	12·3	23·2	39·0	42·0	37·5	41·5	42·8
k_2	0·038	0·045	0·037	0·049	0·039	0·053	0·039

We thank the Distillers Company Limited for gifts of styrene, the Chemical Society and Imperial Chemical Industries Limited for grants, and the Governors of Royal Holloway College for financial assistance to one of us (H. B.). The experiments were started at King's College, London.

ROYAL HOLLOWAY COLLEGE (UNIVERSITY OF LONDON),
ENGLEFIELD GREEN, SURREY. [*Received, November 29th*, 1951.]

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317. *Geraniolenes. The Decomposition of 2:6-Dimethylhept-5-en-2-ol and Some Derivatives thereof.*

By L. BATEMAN, J. I. CUNNEEN, and E. S. WAIGHT.

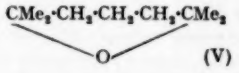
The mixtures obtained by dehydration of 2:6-dimethylhept-5-en-2-ol, by equivalent dehydrohalogenations, and by decarboxylation of geranic acid have been analysed. The first process usually yields olefins containing tetrahydro-2:2:6:6-tetramethylpyran. Pure 2:6-dimethylhepta-2:5-diene has been isolated and characterised. Spectroscopic data on this diene, its $\Delta^{2:6}$-, $\Delta^{2:4}$-, $\Delta^{1:3}$-, and cyclic isomers, and on the above mentioned pyran are reported.

THE nature of the identical or very similar olefinic materials ("geraniolene") obtained by the dehydration of dimethylheptenol (I; X = OH), by decarboxylation of geranic acid, and by other related procedures has remained in doubt from the time of Tiemann

(I) $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2{\cdot}X$ $CH_2{:}CMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}Me$ (II)

and Semmler's original preparation nearly sixty years ago (summarised in Simonsen and Owen, "The Terpenes," Cambridge Univ. Press, 2nd Edn., 1947, pp. 7—9). Difficulty arises because the elimination of HX from (I) can lead to (III), (IV), and alkylated *cyclo*hexenes, and the identification, separation, interconvertability, and proneness to secondary reactions of these isomers have been subject to uncertainty. The possibilities of isomeric

$CMe_2{:}CH{\cdot}CH_2{\cdot}CH{:}CMe_2$ (III) $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH_2$ (IV)

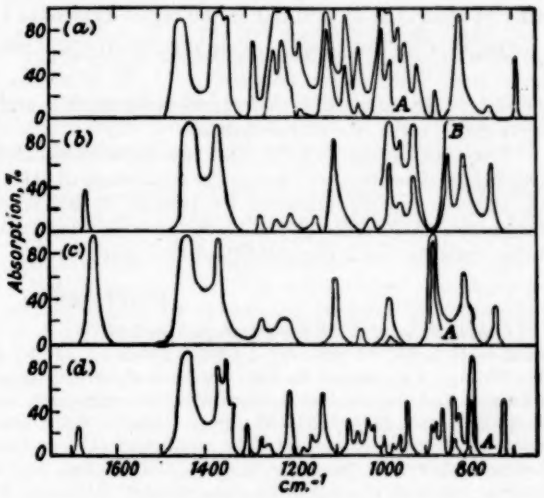


(V)

complexity are further increased if the acyclic monoterpenes are more or less inseparable mixtures of *iso*propylidene and *iso*propenyl structures, *e.g.*, if geranic acid consists of $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CO_2H$ and $CH_2{:}CMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CO_2H$, and the methylheptenone which is the precursor of (I) is admixed with (II) (Simonsen and Owen, *op. cit.*, pp. 2—4; cf. also Grignard and Doeuvre, *Bull. Soc. chim.*, 1929, [iv], **45**, 809). The latter complication, however, can now be disregarded as physico-chemical investigations have recently established that no detectable proportion of the *iso*propenyl form occurs in the natural compounds of present interest (Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland, *J.*, 1950, 915). Furthermore, the infra-red spectroscopic method of structure analysis, soundly based in the acyclic terpene field, now provides a more direct and unequivocal means of recognising and estimating isomeric olefins than the older methods involving oxidative degradation (Barnard *et al.*, *loc. cit.*). By this means, the compositions of several geraniolene preparations have been determined approximately

quantitatively, and earlier inferences (Auwers and Moosbrügger, *Annalen*, 1912, **387**, 183; Simonsen and Owen, *op. cit.*, pp. 8—9) that these are invariably heterogeneous are confirmed. Our primary purpose of isolating pure (III) has been realised; its particularly interesting autoxidation characteristics will be described elsewhere.

Dehydration of (I; X = OH) with a number of reagents yields products which after repeated distillation from sodium fail to give analyses accurate for C_9H_{16} and contain 0·5—2·0% of oxygen; iodine is exceptional in giving a figure as high as 6% (see Experimental). The infra-red spectra show strong absorption at 885 and 1650 cm.$^{-1}$, indicating the presence of $CR_2{:}CH_2$ groups (Barnard *et al.*, *loc. cit.*) and thus that (IV) is a major constituent, and weaker absorption at 815 cm.$^{-1}$ (associated with $CR_2{:}CHR$ groupings); they fail to specify any functional groups attributable to the oxygenated material. This material must therefore be either bismethylheptenyl ether or tetrahydro-2 : 2 : 6 : 6-tetramethylpyran (V). The pyran is the known " methylcinene " (Rupe and Schlochoff, *Ber.*, 1905, **38**, 1498); it has almost the same boiling point as the dehydration product and was virtually proved to be the contaminant by elementary analysis and unsaturation



Infra-red absorption spectra. Path-length, 0·05 mm., except where indicated A (0·01 mm.) or B (0·1 mm).

a, 2 : 2 : 6 : 6-*Tetramethyltetrahydropyran.*
b, 2 : 6-*Dimethylhepta*-2 : 5-*diene.*
c, 2 : 6-*Dimethylhepta*-2 : 6-*diene.*
d, cyclo*Geraniolene.*

data. Rigorous proof was provided by infra-red spectral comparisons (cf. Fig. 1*a* for the pure compound). Its formation finds analogies in other terpenoid and *pseudo*-terpenoid systems (see Clemo and Davison, *J.*, 1951, 447), but was overlooked in the present example by the earlier workers.

Sometimes, and inexplicably, a non-oxygen containing olefin C_9H_{16} was obtained on dehydration with anhydrous oxalic acid; this was found to consist largely of *cyclo*geraniolene (possibly α- and β-) admixed with acyclic heptadienes (cf. Harries and Weil, *Ber.*, 1904, **37**, 848).

Differing from the above, pyrolysis of geranic acid and of dimethylheptenyl acetate (I; X = OAc) and dehydrohalogenation of the corresponding chloride or bromide (I; X = Cl or Br), yield mixtures of (III) and (IV). The product from geranic acid consists almost entirely of (IV) (contrast Grignard and Doeuvre, *loc. cit.*) whereas more nearly equal quantities result from the other reactions. The infra-red spectra of, for example, the dehydrohalogenation products are distinctly " cleaner " than those of the dehydration products. The pure components were isolated by fractionation of such mixtures through a 40-plate column, and were characterised by their infra-red spectra (Figs. 1*b* and *c*) and by the following properties: (III), b. p. 150—151°/756 mm., n_D^{20} 1·4490; (IV), b. p. 141—142°/756 mm., n_D^{20} 1·4388; those of (IV) were in excellent agreement with Henne and Chanan's data for a synthetic specimen (*J. Amer. Chem. Soc.*,

1944, **66**, 392). The difference in n_D affords the simplest means of analysing the composition of a binary mixture: when (V) or similar substances are present, the proportion of (IV) may be determined from the absorption intensity at 885 cm.$^{-1}$, or (III) may be estimated from the amount of conjugated diene produced by hot alkali, as discussed below.

When (III) is heated with potassium hydroxide in methyl alcohol at 165°, isomerisation occurs and light absorption properties are finally developed ($\lambda_{max.}$ 2370 Å, $\varepsilon = 26{,}100$) which empirical reasoning associates with the 1 : 1 : 4-trialkylbutadiene (VI) (Booker, Evans, and Gillam, *J.*, 1940, 1453; Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72).* This extensive conjugative change is to be contrasted with the equlilibrium $Ph{\cdot}CH_2{\cdot}CH{:}CMe_2$ (43%) $\rightleftharpoons$ $Ph{\cdot}CH{:}CH{\cdot}CHMe_2$ (57%) prevailing under the same conditions (Bateman and Cunneen, *J.*, 1951, 2283), and reflects the substantially greater resonance energy of the butadienoid compared with the styryl unit. It is of interest that (VI) could not be obtained from the alcohol (VII), which on dehydration yields an olefinic mixture consisting largely of (VIII), this behaviour simulating that of the quaternary salts of analogous bromides (Bateman, Cunneen, and Koch, *J.*, 1950, 3051). A concentrated fraction of (VIII) showed maximum ultra-violet light absorption at a wave-length (2300 Å, $\varepsilon = 23{,}000$) significantly shorter than that of (VI) but in the region typical of 1 : 3-dialkylbutadienes (Booker *et al.*,

$CMe_2{:}CH{\cdot}CH{:}CH{\cdot}CHMe_2$ (VI) $\quad$ $CMe_2{:}CH{\cdot}CH(OH){\cdot}CH_2{\cdot}CHMe_2$ (VII) $\quad$ $CH_2{:}CMe{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CHMe_2$ (VIII)

loc. cit.). The structural distinction between (VI) and (VIII) is further indicated by their infra-red spectra (see Experimental).

The compounds (IV), (V), and any cyclic mono-olefins are inert under the isomerisation conditions described, and hence the percentage of (III) in a mixture containing one or more of these is readily obtained as $100E^{1\%}_{1\,cm.}/2100$, where $E^{1\%}_{1\,cm.}$ expresses the absorption intensity as 2370 Å developed on the isomerisation treatment. Several synthetic mixtures were tested to check the validity of this procedure.

Experimental

Dehydration of 2 : 6-*Dimethylhept-5-en-2-ol* (I; X = OH).—This structurally homogeneous alcohol, b. p. 75°/12 mm., n_D^{20} 1·4492 (Found: C, 75·9; H, 12·7. Calc. for $C_9H_{18}O$: C, 76·0; H, 12·7%), was heated at 140° with the dehydrating agent (at 180° with boric acid) under nitrogen, and the product isolated by ether-extraction, and finally distilled at least twice from sodium (b. p.'s 139—145°/760 mm.). Details of the experimental conditions and of the products are given in the table. The amount of (IV) present varied in the different preparations, but was always of the order of 50% (as indicated by the absorption intensity at 885 cm.$^{-1}$). On fractionation through a 15-plate column, (IV) and (V) tended to concentrate in the lower-boiling fractions, but these ternary mixtures proved unsuitable for separation of the pure components.

Dehydrating agent	Time (hours)	Found n_D^{20}	C, %	H, %	O, % (diff.)	O, % (direct)	Content of (V) (%)
Oxalic acid * ...	1·5	1·4445	85·8	12·9	1·3	1·2	11
Boric acid	3	1·4438	86·8	12·5	0·7	0·5	5
$NaHSO_4$	1	1·4456	86·0	12·8	1·2	—	11
$CuSO_4$	2·5	1·4440	85·6	12·6	1·8	—	16
Ac_2O–$ZnCl_2$ ...	3	1·4449	86·8	12·9	0·3	0·3	3
Iodine †	3	1·4415	81·3	12·7	6·0	—	53

* Irreproducible; see text.

† Product contained approx. 20% of (III), 10% of (IV), and 20% of (VI).

A fractionated specimen from the boric acid treatment, b. p. 142·5—143·0°/757 mm., n_D^{20} 1·4414 (Found: C, 84·8; H, 12·6; O, 2·2%) was hydrogenated over Adams's catalyst: 35·2 mg. absorbed 10·35 ml. of hydrogen at N.T.P. The oxygen content is indicative of a methylcinene (V) content of 20%, the hydrogenation data of a value of 18·8%.

* Previous data on this type of conjugated diene appear to be lacking. Following Ruzicka and van Veen (*Annalen*, 1929, **468**, 143), Booker *et al.* quoted zingiberene as an example, although they were at a loss to explain its low intensity ($\varepsilon = 5300$ at $\lambda_{max.}$ 2355 Å). This sesquiterpene is now known, however, to be quite different in type, *viz.*, an alkenylated *cyclo*hexa-2 : 4-diene (Eschenmoser and Schinz, *Helv. Chim. Acta*, 1950, **33**, 171).

*Tetrahydro-*2 : 2 : 6 : 6-*tetramethylpyran* ("*Methylcinene*").—Prepared according to the directions of Rupe and Schlochoff (*loc. cit.*), this compound had b. p. 143°/762 mm., n_D^{20} 1·4287 (Found : C, 76·0; H, 12·7. Calc. for $C_9H_{18}O$: C, 76·0; H, 12·7%).

Formation of cyclo*Geraniolene during the Dehydration of Dimethylheptenol* (I; X = OH).—The heptenol (5 g.) was heated with anhydrous oxalic acid (2 g.) at 140° for 1·5 hours. The isolated product (3·5 g.) had b. p. 138—141°/761 mm., n_D^{20} 1·4476 (Found : C, 86·9; H, 12·9%); 45 mg. absorbed 10·8 ml. of hydrogen at N.T.P., corresponding to $|^{=}$ 1·33 for C_9H_{16}. Its infra-red spectrum was very similar to that of a mixture of *cyclo*geraniolene prepared as below (70%) and equal proportions of the dimethylhepta-2 : 5- and -2 : 6-diene; (V) was absent. The reason for the variable dehydrating action of oxalic acid remains obscure; traces of moisture in the acid do not appear to be reponsible.

Pyrolysis of 2 : 6-*Dimethylhept-5-enyl Acetate* (I; X = OAc).—Prepared from the corresponding alcohol by acetic anhydride and zinc chloride, this acetate had b. p. 89—91°/13 mm., n_D^{20} 1·4382 (cf. Escourrou, *Bull. Soc. chim.*, 1926, **39**, 1121). On passage in a stream of nitrogen through a 75-cm. tube packed with glass wool at 480° during 15 hours, it yielded an olefin with b. p. 140—142°/757 mm., n_D^{20} 1·4412 (Found : C, 86·9; H, 12·9%). Infra-red spectroscopic examination confirmed the absence of methylcinene and indicated a 2 : 6-diene content consistent with the refractive index (77%; see p. 1715).

Decarboxylation of Geranic Acid.—The acid (30 g.), b. p. 108°/0·1 mm., n_D^{20} 1·4886 (containing <3% of $CR_2{:}CH_2$ groups, probably nil), was heated at atmospheric pressure so that a distillate passed over at <150°. After being dissolved in ether, washed with water, dried, freed from solvent, and distilled from sodium, the product (20 g.) had b. p. 141—143°/759 mm., n_D^{20} 1·4392 (Found : C, 87·1; H, 12·9%). The refractive index indicates a mixture of 96% of (IV) and 4% of (III) (see p. 1715), and consistently the infra-red spectrum was practically identical with that of pure (IV) (Fig. 1*c*).

cyclo*Geraniolene.*—A portion of the above specimen of geraniolene (essentially IV) was shaken with sulphuric acid for 8 hours (Wallach and Franke, *Annalen*, 1902, **324**, 114). The resulting *cyclo*geraniolene had b. p. 136—137°/765 mm., n_D^{20} 1·4457 [Found : C. 86·5; H, 12·9%; $|^{=}$ (hydrogenation), 0·97]. Its infra-red spectrum (Fig. 1*d*) is in accord with the α- or β-structure.

Dehydrochlorination of 6-*Chloro-*2 : 6-*dimethylhept-2-ene* (I; X = Cl).—This *chloride*, prepared in 42% yield from the corresponding alcohol by Hatch and Nesbitt's procedure (*J. Amer. Chem. Soc.*, 1950, **72**, 729), had b. p. 71—72°/15 mm., n_D^{20} 1·4493 (Found : C, 67·2; H, 10·6; Cl, 22·4. $C_9H_{17}Cl$ requires C, 67·3; H, 10·6; Cl, 22·2%). Its infra-red spectrum confirmed the absence of other than trisubstituted ethylene groupings. Some spontaneous dehydrochlorination occurred during this preparation, yielding as a forerun an olefin mixture (13%) rich in (III), b. p. 144—147°/753 mm., n_D^{20} 1·4463 (Found : C, 86·9; H, 13·0%). Deliberate dehydrochlorination was effected by heating the chloride (156 g.) with purified pyridine (350 ml.) at 140° for 20 hours. The crude olefinic product (108 g.) was distilled from sodium (Found : C, 86·9; H, 13·0%; $|^{=}$ (hydrogenation), 1·98. Calc. for C_9H_{16} : C, 87·0; H, 13·0%; $|^{=}$, 2·00) and then fractionated through a 40-plate column to yield : (i) 2 : 6-dimethylhepta-2 : 6-diene (37 g.), b. p. 141—142·0°/756 mm., n_D^{20} 1·4388 (Found : C, 86·9; H, 12·9%); (ii) (24 g.), b. p. 142·1—147·5°/754 mm., n_D^{20} 1·4414; (iii) (8 g.), b. p. 147·6—148·2°/754 mm., n_D^{20} 1·4472; (iv) (6 g.), b. p. 148·3°/754 mm.; (v) (20 g.), residue. The 2 : 5-diene contents of fractions (ii), (iii), and (iv) were 73, 12, and 3% respectively, as determined by infra-red analysis. On distillation of (v) from a small flask, 2 : 6-*dimethylhepta-*2 : 5-*diene* was obtained, of b. p. 150—151°/758 mm., n_D^{20} 1·4490 (Found : C, 86·9; H, 12·9%; $|^{=}$, 2·01); contamination with its $\Delta^{2:6}$-isomer was <0·1%.

6-*Bromo-*2 : 6-*dimethylhept-2-ene* (I; X = Br).—The action of phosphorus tribromide (73 g.) on the corresponding alcohol (56 g.) gave this *bromide*, b. p. 76—77°/11 mm., n_D^{20} 1·4711 (Found : C, 52·6; H, 8·2; Br, 38·3. $C_9H_{17}Br$ requires C, 52·7; H, 8·3; Br, 39·0%), in rather poor yield (15%). It undergoes dehydrobromination in pyridine at 140°, to give an olefinic mixture similar to that obtained from the chloride (n_D^{20} 1·4431) (Found : C, 87·0; H, 12·9%).

Isomerisation of 2 : 6-*Dimethylhepta-*2 : 5-*diene.*—When the pure 2 : 5-diene was heated with methyl alcoholic potash at 165° (Bateman and Cunneen, *loc. cit.*), light absorption at 2370 Å steadily increased and reached a maximum after about 100 hours with ε = 26,100. Various olefinic mixtures behaved as follows :

Mixture	(III) 40% + (IV) 60%	(III) 70% + (IV) 30%	(III) 25% + (IV) 55% + (V) 20%
$E_{1\,cm.}^{1\%}$ at 2370 Å	837	1520	478
2 : 5-Diene content, estimated, %	40	72	23

Isolated from a large-scale isomerisation, (VI) had n_D^{20} 1·4650, and exhibited infra-red absorption at 814 and 958 cm.$^{-1}$, attributable to the presence of $CR_2{:}CHR$ and *trans*-CHR:CHR groups respectively.

2 : 6-*Dimethylhepta*-1 : 3-*diene*.—2 : 6-*Dimethylhept*-2-*en*-4-*ol*, b. p. 74—76°/12 mm., n_D^{20} 1·4410 (Found : C, 75·6; H, 12·7. $C_9H_{18}O$ requires C, 76·0; H, 12·7%), was obtained from β-methylcrotonaldehyde (Fischer, *Ber.*, 1943, **76**, 734) and *iso*butylmagnesium bromide. Dehydration of this alcohol with sodium hydrogen sulphate at 140° afforded the slightly impure 1 : 3-diene, b. p. 66°/13 mm., n_D^{20} 1·4569, $\varepsilon_{max.}$ (unchanged in hot alkali at 165° for 100 hours) = 23,000 at 2300 Å (Found : C, 86·0; H, 13·2%). Its infra-red spectrum showed strong absorption at 888 and 961 cm.$^{-1}$ attributable to the presence of $CR_2{:}CH_2$ and *trans*-CHR:CHR groupings, respectively (contrast the $\Delta^{2:4}$-isomer).

Spectroscopic Measurements.—The infra-red absorption spectra were determined with a Grubb-Parsons single-beam instrument, with the technique previously described (Barnard, Fabian, and Koch, *J.*, 1949, 2442). The ultra-violet absorption spectra were measured in ethanolic solution with either a Hilger Uvispek photoelectric spectrophotometer or a Hilger Small Quartz spectrometer and Spekker photometer by the usual methods.

This work forms part of a programme of fundamental research undertaken by the Board of the British Rubber Producers' Research Association.

48, Tewin Road, Welwyn Garden City. [*Received, December 20th*, 1951.]

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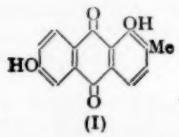
318. *Chemistry of the* Coprosma *Genus. Part VI.* Minor Anthraquinone Colouring Matters from* Coprosma australis.

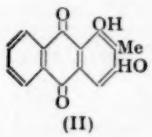
By Lindsay H. Briggs, G. A. Nicholls, and R. M. L. Paterson.

Three further compounds, soranjidiol, rubiadin, and a new dihydroxydimethoxymethylanthraquinone, have been isolated in small yield from the stem-bark of *Coprosma australis*. The new compound is shown to be copareolatin 1(or 5) : 6-dimethyl ether (*vide infra* for corrected nomenclature).

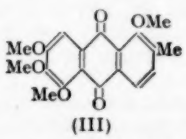
In working up the acetone extract of the stem-bark of *Coprosma australis* for its known constituents, morindin, morindone, and rubiadin 2-methyl ether (Part I, *J.*, 1948, 564) by chromatography on magnesia columns and using the displacement technique with acetic acid as described in Parts IV (*J.*, 1949, 1241) and V,* we have obtained, with difficulty, three further minor constituents. Two have been identified with the known compounds, soranjidiol (1 : 6-dihydroxy-2-methylanthraquinone) (I) and rubiadin (1 : 3-dihydroxy-2-methylanthraquinone) (II) respectively. The third compound is a new compound, $C_{17}H_{14}O_6$, containing two hydroxyl and two methoxyl groups, related to our " areolatin " † since complete methylation afforded the tetramethyl ether thereof (III). This new



(I)



(II)



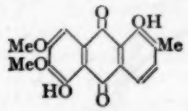
(III)

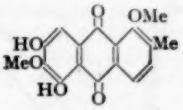
dimethyl ether is isomeric with copareolatin dimethyl ether prepared by partial methylation of copareolatin (Part II, *loc. cit.*), which we consider is the 6 : 7-dimethyl ether (IV). It dissolves in sodium carbonate solution, indicating a free β-hydroxyl group, and 80% sulphuric acid at 100° demethylates only one methoxyl group which must therefore be in

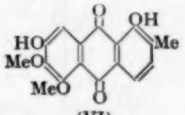
* Part V, *J.*, 1949, 1246.

† In Part II (*J.*, 1948, 568) a new compound, $C_{15}H_{10}O_6$, was isolated from *Coprosma areolata* and shown by degradation and synthesis (Part III, *J.*, 1948, 990) to be 1 : 5 : 6 : 7-tetrahydroxy-2-methylanthraquinone, for which the name areolatin was proposed. It was unfortunately not noticed, however, that the same name had been given by Hesse (*J. pr. Chem.*, 1903, **68**, 1) to a compound of unknown structure from *Pertusaria rupestris* [*P. communis* (β) *areolata*] with which it is not identical. We now propose the name copareolatin for the above compound from *Coprosma areolata*.

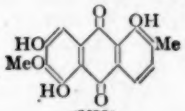
the α-position (cf. Graebe, *Annalen*, 1906, **349**, 211). These two facts, therefore, indicate the presence of methoxyl groups in α- and β-positions. Both the dimethyl ether and the monomethyl ether derived from it by demethylation are displaced by acetic acid on the magnesia column during chromatography, which indicates, in our experience, the absence of a vicinal dihydroxy-configuration. For these reasons, the dimethyl ether must be the 1(or 5) : 6-dimethyl ether (V) [or (VI)], while the monomethyl ether must be the 6-methyl ether (VII).

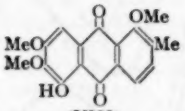

(IV)

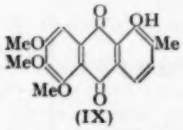

(V)


(VI)

On chromatography of a preparation of copareolatin 6 : 7-dimethyl ether (Part II, *loc. cit.*), a trimethyl ether has been isolated, which is most probably the 1 : 6 : 7- or the 5 : 6 : 7-trimethyl derivative, (VIII) or (IX), the two β-hydroxyl groups undergoing methylation before the α-hydroxyl groups. From stereochemical considerations, however, the methoxyl group being larger than a methyl group, we suggest that, of the two α-hydroxyl groups, the one in the 1-position would be preferably methylated, leading to (VIII) for the trimethyl ether.


(VII)


(VIII)


(IX)

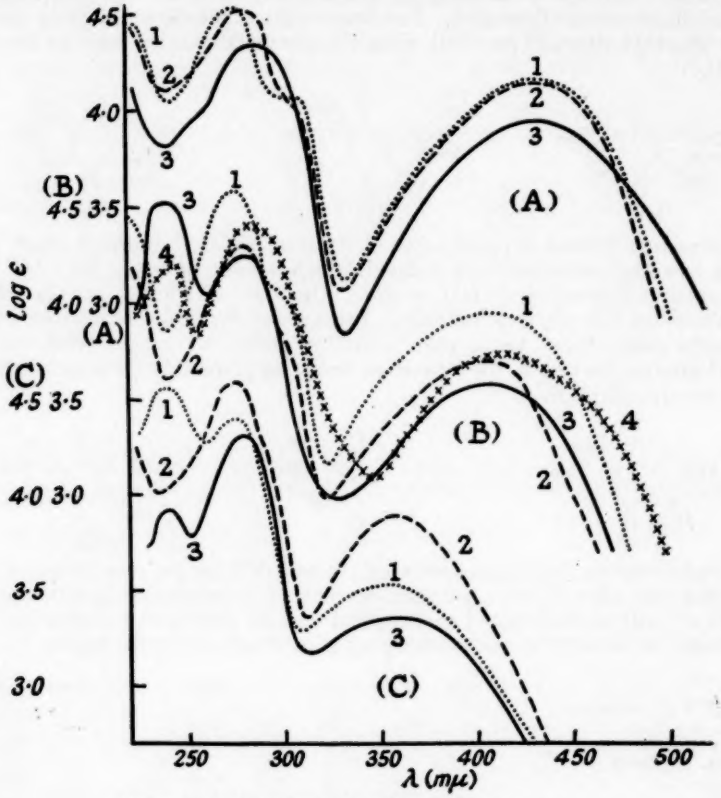
In an endeavour to differentiate between (V) and (VI) for the new dimethyl ether we have studied the ultra-violet absorption spectra of copareolatin and its methylated derivatives as well as the related anthragallol and its methylated derivatives. These measurements are recorded in the following table (λ in mμ) and in the figure.

	λ	log ε	λ	log ε	λ	log ε	λ	log ε	λ	log ε
Anthragallol 1 : 2-dimethyl ether	—	—	241	3·92	281	4·30	—	—	362·5	3·36
Anthragallol trimethyl ether	—	—	240	4·55	276·5	4·40	—	—	356	3·53
Copareolatin tetramethyl ether	—	—	—	—	276	4·59	—	—	358	3·88
Anthragallol	—	—	245·5	4·21	283·5	4·40	335 *	~3·21	413·5	3·72
„ 2-methyl ether	—	—	240	4·51	281·5	4·24	—	—	407·5	3·57
Copareolatin 1(or 5) : 6 : 7-trimethyl ether	—	—	—	—	276·5	4·57	300 *	~4·04	411	3·93
Copareolatin 1(or 5) : 6-dimethyl ether	—	—	—	—	281·5	4·29	—	—	407·5	3·68
Copareolatin	—	—	258 *	~3·96	288·5	4·34	—	—	432·5	3·92
„ 6-methyl ether	—	—	—	—	280	4·51	305 *	~4·05	432	4·11
„ 6 : 7-dimethyl ether	224·5	4·44	—	—	276	4·52	305 *	~4·04	427·5	4·13

* Inflexion.

Anthragallol and all of its derivatives exhibit an absorption band in the region 240—245·5 μ (log ε 3·92—4·55), not shown by copareolatin and its derivatives. This absorption is due to the chromophore $-C_6H_4\cdot COR$, one of the fundamental bands of anthraquinone itself (Morton and Earlam, *J.*, 1941, 159). A second band, also characteristic of this chromophore, is present only in the spectrum of anthragallol itself and then only as an inflexion at 335 mμ (log ε *ca.* 3·21). All compounds exhibit absorption in the region 276—288·5 mμ (log ε 4·24—4·59), characteristic of the quinonoid nucleus of anthraquinone itself (Morton and Earlam, *loc. cit.*). All the compounds exhibit a further broad absorption band due to the carbonyl group of the quinonoid nucleus, falling into three distinct groups at 356—362·5 (log ε 3·36—3·88), 407·5—413·5 (log ε 3·57—3·93), and 427·5—432·5 mμ (log ε 3·92—4·13). An inspection of the formulæ of these compounds reveals that the

common feature in the first group is that they contain no free α-hydroxyl group, in the second that they contain one free α-hydroxyl group, and in the third that they contain two such groups. Apparently this major band is greatly affected by the number of



Group A : 1. *Copareolatin* 6 : 7-*dimethyl ether.*
2. *Copareolatin* 6-*methyl ether.*
3. *Copareolatin.*

Group B : 1. *Copareolatin* 1(*or* 5) : 6 : 7-*trimethyl ether.*
2. *Copareolatin* 1(*or* 5) : 6-*dimethyl ether.*
3. *Anthragallol* 2-*methyl ether.*
4. *Anthragallol.*

Group C : 1. *Anthragallol trimethyl ether.*
2. *Copareolatin tetramethyl ether.*
3. *Anthragallol* 1 : 2-*dimethyl ether.*

α-hydroxyl groups, the presence of β-hydroxyl groups having little effect. Similar observations have been made by Morton and Earlam (*loc. cit.*).

It is not possible to differentiate between (V) and (VI) on the above data.

Experimental

The crude pigment from the stem bark of *Coprosma australis* was extracted with boiling acetone and cooled. A waxy substance separated which was removed before chromatography of the remaining acetone solution on six columns (4·5 × 16 cm.) of freshly calcined magnesia. At first the chromatogram resembled that described in Part I (*loc. cit.*) except that there was no band corresponding to morindin which had apparently been removed at an earlier stage. On development, however, and particularly on the addition of acetic acid (1—2 c.c. in 10—20 c.c.

of acetone) followed by further development with acetone, three relatively small bands were displaced with great difficulty from the strongly absorbed morindone band. The acetic acid drew the morindone down the column at the same time as the three smaller bands were displaced, making a clear cut separation impossible by a single absorption. The columns were extruded, and the three smaller, overlapping bands were cut out and finally separated into homogeneous bands by repeated chromatography on columns of decreasing size as described in Part IV (*loc. cit.*).

Band I : Morindone.—This was isolated and identified as described in Part I (*loc. cit.*).

Band II : Copareolatin 1(or 5) : 6-*Dimethyl Ether.*—The magnesia was removed from this band by dissolution in hydrochloric acid and the liberated pigment crystallised from glacial acetic acid (charcoal), forming orange hexagonal plates which darken, sublime, and sinter before melting at 271° (Found : C, 64·7; H, 4·4; OMe, 16·6. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5; 2OMe, 19·7%). The *compound* is soluble in 10% sodium hydroxide and sodium carbonate solutions with an orange-red colour, soluble in concentrated sulphuric acid with a violet colour, and gives a brown colour with ferric chloride solution.

The *diacetate* was prepared by momentarily warming over a water-bath a mixture of the dimethyl ether (24 mg.), acetic anhydride (0·5 c.c.), and 60% perchloric acid (1 drop) and pouring the whole into water 10 minutes later. The insoluble diacetate crystallised from alcohol in pale cream-coloured needles of constant decomposition point 131° when slowly heated (Found : C, 63·3; H, 4·5. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·55%).

The dimethyl ether was completely methylated with methyl sulphate and anhydrous potassium carbonate in acetone solution and formed pale yellow needles, m. p. 182—183°, when crystallised from alcohol, undepressed by an authentic sample of copareolatin tetramethyl ether, m. p. 184—185°. The latter compound was purified by chromatography and has a higher m. p. than that recorded in Part II (*loc. cit.*).

The dimethyl ether (90 mg.) was partly demethylated by 80% sulphuric acid (7 c.c.) for 1½ hours at 100° (cf. Graebe, *Annalen*, 1906, **349**, 222). At first the solution had a clear bright red colour but gradually a red precipitate was formed. The orange-yellow material obtained on dilution with water (10 c.c.) was dissolved in acetone and chromatographed on magnesia. Three bands were obtained : the small top band probably contained copareolatin ; the bottom band contained unchanged material (16 mg.), recovered as orange plates, m. p. 271—272°, from glacial acetic acid ; the intermediate red band afforded *copareolatin 6-methyl ether* (50 mg.), crystallising from glacial acetic acid in orange needles of constant m. p. 241° (Found : C, 64·2; H, 4·25. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%). The monomethyl ether is soluble in 10% sodium hydroxide and sodium carbonate solutions with a red colour and gives a brown colour with ferric chloride.

Band III : Soranjidiol (1 : 6-*Dihydroxy-2-methylanthraquinone*).—The yellow pigment recovered from this band was repeatedly crystallised from glacial acetic acid, forming orange-yellow needles, m. p. and mixed m p. with 1 : 6-dihydroxy-2-methylanthraquinone *ex C. acerosa* (Part V, *J.*, 1949, 1246), 287—288°.

Band IV : Rubiadin (1 : 3-*Dihydroxy-2-methylanthraquinone*).—The yellow pigment recovered from this band crystallised from glacial acetic acid as yellow plates, m. p. and mixed m. p. with rubiadin, *ex C. lucida* (Part IV, *loc. cit.*), 297°. The acetate (cf. Part IV) crystallised from acetic anhydride as pale yellow needles, m. p. and mixed m. p. with rubiadin diacetate, 235°.

Band V : Rubiadin 1-*Methyl Ether.*—This was isolated and identified as described in Part I (*loc. cit.*).

Copareolatin 1(*or* 5) : 6 : 7-*Trimethyl Ether.*—A preparation of copareolatin 6 : 7-dimethyl ether (Part II, *loc. cit.*) was dissolved in acetone and chromatographed on magnesia. Three bands were obtained, two top red bands, one much darker than the other, but from both of which copareolatin 6 : 7-dimethyl ether was recovered, and an orange band. From the last band *copareolatin* 1(*or* 5) : 6 : 7-*trimethyl ether* was recovered and crystallised from alcohol as yellow needles of constant m. p. 177—178° (Found : C, 65·6; H, 5·2; OMe, 29·7. $C_{18}H_{16}O_6$ requires C, 65·8; H, 4·9; 3OMe, 28·4%). The trimethyl ether is insoluble in sodium carbonate solution but dissolves in 10% sodium hydroxide solution with a red colour and gives a brown colour with ferric chloride. On methylation with methyl sulphate and potassium carbonate in acetone solution it afforded copareolatin tetramethyl ether, crystallising from alcohol in pale yellow needles, m. p. 180°, undepressed by an authentic specimen.

The absorption spectra were measured in *ca.* N/20,000-alcoholic solution in a Beckman spectrophotometer, Model DU. All the compounds were rigidly purified by chromatography

from acetone solutions on magnesia columns until pure chromatograms were obtained, and then crystallised from appropriate solvents.

The analyses are by Drs. Weiler and Strauss, Oxford, Dr. T. S. Ma, Microchemical Department, Otago University, Dunedin, and Mr. R. N. Seelye of this department.

We are indebted to the Chemical Society, the Australian and New Zealand Association for the Advancement of Science, the Royal Society of New Zealand and the Research Fund Committee of the University of New Zealand for grants and, for one of us (G. A. N.), for a Research Fund Fellowship.

AUCKLAND UNIVERSITY COLLEGE, AUCKLAND,
NEW ZEALAND. [*Received, December 20th*, 1951.]

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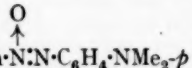
319. *Condensation of* N-*Phenylhydroxylamine with* NN-*Dimethyl*-p-*nitrosoaniline. The Azoxy-compounds derived from* p-*Dimethylaminoazobenzene.*

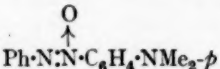
By W. ANDERSON.

α- and β-*p*-Dimethylaminoazoxybenzene (I and II) are both obtained on condensation of *N*-phenylhydroxylamine with *NN*-dimethyl-*p*-nitrosoaniline. Absorption-spectrum measurements were used to assign the structures to the compounds. The course of the reaction, which was studied in some detail, was contrary to that generally found for reactions between *N*-arylhydroxylamines and arylnitroso-compounds possessing different aryl residues.

THE main object of the present investigation was the preparation of the isomeric azoxy-compounds (I) and (II) derived from *p*-dimethylaminoazobenzene. Direct oxidation of



α-Isomer (I)



β-Isomer (II)

the azo-compound with peracetic acid is unsuitable, since according to Angeli (*Atti R. Accad. Lincei*, 1915, **24**, 1190) it leads to the amine oxide of (II). Furthermore, interaction of *N*-arylhydroxylamines and arylnitroso-compounds possessing different aryl residues generally produces symmetrical azoxy-compounds (Bamberger and Renauld, *Ber.*, 1897, **30**, 2278; Renauld, Thesis, Rennes, 1896; Bamberger, *Viert. Naturforsch. Gess. Zürich*, 1896, **41**, 174; Müller, *Annalen*, 1932, **495**, 132; Taylor and Baker in Sidgwick's "Organic Chemistry of Nitrogen," Oxford Univ. Press, 1942, p. 427). This has been represented as a process of mutual oxidation and reduction:

$$2NHAr{\cdot}OH + 2Ar'{\cdot}NO \longrightarrow Ar{\cdot}N_2O{\cdot}Ar + Ar'{\cdot}N_2O{\cdot}Ar' \quad . \quad . \quad . \quad . \quad (1)$$

There were indications however that the compounds desired might be formed in a hydroxylamine–nitroso-compound reaction. Thus, Bamberger and Bernays (*Ber.*, 1902, **35**, 1624) obtained one of the isomeric *p*-hydroxyazoxybenzenes from *N*-phenylhydroxylamine and *p*-nitrosophenol. Bamberger and Renauld (*loc. cit.*) suggested that unsymmetrical compounds, although not isolated, may have been present as products of other reactions of this type. Of interest also was that the rate of formation of azoxy-compounds is greatly increased by alkali (see Brand and Mahr, *J. pr. Chem.*, 1931, **131**, 97; 1935, **142**, 153). The following scheme analogous to that for the aldol-type condensation has been proposed:

$$NHAr{\cdot}OH + Ar{\cdot}NO \longrightarrow HO{\cdot}NAr{\cdot}NAr{\cdot}OH \longrightarrow ArN{\overset{\uparrow}{\underset{O}{:}}}NAr + H_2O \quad . \quad . \quad (2)$$

This alkali effect seems to have been studied only in reactions with hydroxylamines and nitroso-compounds possessing the same aryl residue; other reactions have generally been

conducted in neutral solution. In the present work the reaction of *N*-phenylhydroxylamine with *NN*-dimethyl-*p*-nitrosoaniline was studied under various reaction conditions.*

When *N*-phenylhydroxylamine condensed with dimethyl-*p*-nitrosoaniline in alcohol in the presence of alkali, chromatography of the crude reaction product yielded two pale orange crystalline substances, m. p. 126·2—126·6° and 122·5—123·2° respectively, further characterised as their picrates. The separation on the column was quite definite and the melting points were strongly depressed on admixture. The substances were shown to be the azoxy-compounds (I) and (II).

The substances were soluble in warm dilute acids, giving colourless or slightly pink solutions. White crystalline hydrochlorides were formed under anhydrous conditions but sulphates were not obtained, presumably owing to their ready hydrolysis. Subjected to the Wallach reaction (Taylor and Baker, *op. cit.*, p. 428), both isomers yielded *p*-dimethylamino-*p'*-hydroxyazobenzene almost quantitatively. Most reactions of this type have been applied to only one compound of an isomeric pair although rearrangements of both to the same phenol are not unknown (Angeli, *Gazzetta*, 1916, **46**, ii, 82). On reduction, both substances gave *p*-dimethylaminoazobenzene.

Absorption spectra (see below) provide good evidence that the substance with m. p. 126·2—126·6° is the α-isomer (I) and that with m. p. 122·5—123·2° is the β-isomer (II). The spectra also show that both compounds possess the *trans*-azo-configuration. This is confirmed by the stability of the compounds at temperatures well above their melting points.

The isolation of the α- and the β-azoxy-compound discussed above appears to be the first example of a reaction of this type from which both isomers have been obtained. It is in keeping with the theoretical scheme (2). The reaction was studied more fully both in presence and in absence of alkali, in order to provide a comparison with similar reactions where the scheme (1) appears to apply.

In the reaction in presence of alkali the following substances were isolated: α- and β-*p*-dimethylaminoazoxybenzene, large quantities of azoxybenzene, a small quantity of *pp'*-bisdimethylaminoazoxybenzene, a trace of azobenzene, and a small impure fraction which may have been *pp'*-bisdimethylaminoazobenzene. The reaction without alkali, under the conditions used by Bamberger and Bernays (*loc. cit.*) for hydroxylamine–nitroso-compound reactions, gave the same products with a small amount of *p*-dimethylaminoazobenzene in addition; the yields of the azoxy-isomers were considerably smaller.

The occurrence of large amounts of azoxybenzene was due to the direct decomposition of the *N*-phenylhydroxylamine, and the other symmetrical azoxy-compound was only a trace product of the reaction. It would thus appear that the oxidation–reduction mechanism plays a very minor role in the interaction of *N*-phenylhydroxylamine with dimethyl-*p*-nitrosoaniline. Condensation proceeds, giving the unsymmetrical compounds, and this is aided by the presence of alkali.

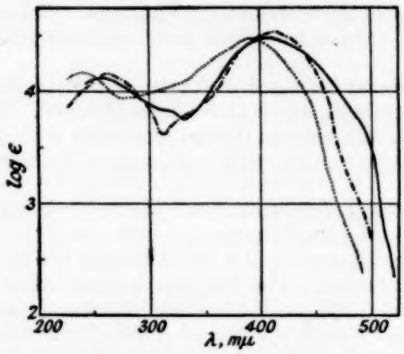
The course of the reaction is in sharp contrast to that generally accepted for similar hydroxylamine–nitroso-compound reactions. This may be in part only apparent since the reaction products are always complex and information obtained from separations dependent on fractional crystallisation, as used in previous studies, is less complete than that gained by employing chromatography. However, there is no doubt that the production of symmetrical compounds is in general an important feature of these reactions. It is significant that in most cases nuclear-substituted *N*-phenylhydroxylamines were caused to react with nitrosobenzene. A study of the decomposition of nitrosobenzene under the conditions employed by Bamberger *et al.* for the production of azoxy-compounds, but without the addition of the hydroxylamine, showed that 15% of the nitrosobenzene was converted into azoxybenzene. This fact and the probability of similar decomposition of hydroxylamines indicate that the production of symmetrical azoxy-compounds is at least

* The following errors in the literature should be noted. (1) Bigelow (*Chem. Reviews*, 1931, **9**, 157) states that Fischer and Wacker (*Ber.*, 1888, **21**, 2609) condensed dimethyl-*p*-nitrosoaniline with phenylhydroxylamine in absolute alcohol, obtaining *p*-azoxydimethylaniline. The reaction actually conducted was a condensation of dimethyl-*p*-nitrosoaniline with phenylhydrazine in absolute ether. (2) In *Chem. Abs.*, 1936, **30**, 9996, 2934[8], a substance listed as "Aniline, *NN*-dimethylphenylazoxy," $C_{14}H_{15}N_3O$ (Bigiavi and Albanese, *Gazzetta*, 1935, **65**, 773), was actually the oxide, $C_{14}H_{15}N_3O_2$, of this substance.

in part independent of any direct interaction of the nitroso-compound and the hydroxylamine. Further assessment of the relative importance of the different processes is prevented by absence, from the literature, of information on the yields of azoxy-compounds obtained. In the present study the nitroso-compound carries a dimethylamino-group, and again in the synthesis of one of the isomeric *p*-hydroxyazoxybenzenes by Bamberger and Bernays (*loc. cit.*) the hydroxyl group was attached to the nitroso-compound. On the other hand, Müller (*loc. cit.*) obtained only symmetrical azoxy-compounds from *o*-bromonitrosobenzene with *N*-*o*-chlorophenylhydroxylamine. The operation of the condensation mechanism in the reactions with the nitrosoaniline and the nitrosophenol may well be related to the profound influence of the amino- and hydroxyl radicals on the structure of these nitroso-compounds (see Taylor and Baker, *op. cit.*, p. 217).

Our intention to study the reaction of nitrosobenzene with *N*-*p*-dimethylaminophenylhydroxylamine has so far not been possible owing to the failure to prepare this hydroxylamine.

Spectrographic Data.—The absorption spectra of the isomers and their parent azo-compound *p*-dimethylaminoazobenzene, measured in 0·01% ethanolic solution, are shown in the Fig. The values for *p*-dimethylaminoazobenzene are in good agreement with those



Absorption of: p-*dimethylaminoazobenzene* ————; *the azoxy-compound, m. p.* 122·5°, ...; *and the azoxy-compound, m. p.* 126°, — · — · —.

recorded by Pongratz *et al.* (*Ber.*, 1938, **71**, 1287) for 0·05% ethanolic solution; there is a slight difference in the $\varepsilon_{max.}$ values of the bands of shorter wave-length.

The features significant to the present work are (1) the similarity for the three compounds of the $\varepsilon_{max.}$ values in the comparable bands, (2) the larger shift of $\lambda_{max.}$ for the azoxy-compound, m. p. 122·5—123·2°, relative to the azo-compound and towards shorter wave-length, and (3) the closer relation of the general shape of the curve of the azoxy-compound, m. p. 126·2—126·6°, to that of the azo-compound.

The first point shows that the isomers possess a *trans*-configuration, since Müller's *cis*-azoxy-compounds (*loc. cit.*; *Annalen*, 1932, **493**, 166) have absorption intensities about half of those of the *trans*-stereoisomers, while the *trans*-compounds have values similar to those of the related azo-compounds. The second and third points together provide strong evidence that the azoxy-compound, m. p. 122·5—123·2°, is the β- and the other the α-isomer. This is based on Szegö's results (*Ber.*, 1929, **62**, 736) for numerous pairs of isomeric azoxy-compounds containing strongly directive groups; both points (2) and (3) are characteristic features of Szegö's spectra.

Experimental

Spectra were measured with a Hilger " Spekker " photometer and Medium Quartz Spectrograph, with a condensed spark between tungsten steel electrodes as light source. The recordings were made on Ilford Rapid Panchromatic Process plates, sensitive to 650 mμ. The ethanol employed was purified according to Leighton *et al.* (*J. Amer. Chem. Soc.*, 1931, **53**, 3017). The sample of *p*-dimethylaminoazobenzene, m. p. 117·5—117·8°, had been purified by chromatography.

Light petroleum refers to the fraction of b. p. 60—80°. M. p.s are corrected.

Preparation of the Azoxy-compounds (I *and* II).—*N*-Phenylhydroxylamine was prepared by reduction of nitrobenzene with zinc dust and aqueous ammonium chloride, dried quickly on porous plate, and used immediately. Commercial dimethyl-*p*-nitrosoaniline was recrystallised from light petroleum; this gave material with m. p. 85°.

Solutions of the nitroso-compound (1 g. in 12 c.c.) and the hydroxylamine (2 g. in 12 c.c.) in ethanol were mixed and a few drops of 50% aqueous potassium hydroxide added immediately with shaking. The mixture was heated at 70—80° for 10 minutes, then cooled and poured into water (400 c.c.). After 24 hours in the refrigerator the precipitated material was filtered off and dried, to give a brown powder (1·5 g.). (With some batches the precipitated material was soft and difficult to manipulate. In these cases extraction with benzene proved satisfactory but the chromatogram was more complex. Generally the bulk of the material was precipitated and little was gained by extraction of the diluted mother-liquor.) The brown material was poured on to an alumina column (10 × 1·5″) in benzene; aluminium oxide for chromatographic adsorption analysis supplied by Messrs. British Drug Houses Ltd., Dorset, gave satisfactory separations. The material separated into numerous zones. On development with benzene a broad orange zone appeared, preceded by a trace of yellow-orange material and followed by various orange, scarlet, and other zones. The broad orange zone was finally resolved into two bands which were eluted separately. Each part was subjected to two further chromatographic procedures. The lower band yielded trans-β-p-*dimethylaminoazoxybenzene* (II) (0·17 g.). After sublimation at 135°/0·05 mm. it was obtained from light petroleum as pale yellow-orange needles, m. p. 122·5—123·2° ± 0·3° (Found: C, 69·9; H, 6·2; N, 17·3. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·3; N, 17·4%). The *picrate* prepared and crystallised from ethanol formed stout yellow prisms, m. p. 149—151° (decomp.) (Found: C, 51·2; H, 3·9. $C_{14}H_{15}ON_3,C_6H_3O_7N_3$ requires C, 51·1; H, 3·9%). The upper band yielded the trans-α-*isomer* (I), which was obtained from light petroleum as small pale orange prisms, m. p. 126·2—126·6° ± 0·3° (Found: C, 70·0; H, 6·3; N, 16·9%). The *picrate*, prepared and crystallised from ethanol, formed fine yellow needles, m. p. 155—157° (decomp.) (Found: C, 51·15; H, 3·9%).

The yields recorded are the highest of numerous runs. Similar yields were obtained from reactions at room temperature but the precipitates were finer and difficult to handle. Heating for more than 10 minutes also resulted in fine precipitates. The yields were lower when the hydroxylamine was not in excess of the theoretical quantity.

Chemical Properties of the Azoxy-compounds.—Reactions confirming structures assigned to compounds were as follows.

Hydrochlorides. White crystalline hydrochlorides were obtained by passing dry hydrogen chloride through dry benzene solutions of the materials. These hydrochlorides were quickly hydrolysed in the laboratory atmosphere and unsuitable for routine analysis. Handled with as little exposure to moisture as possible, they did not give sharp m. p.s even in sealed tubes. The hydrochloride of the β-isomer (II) decomposed from 140° to 152°; the other hydrochloride decomposed from 150° to 165°.

Wallach transformation. Solutions of the isomers (0·05 g.) in concentrated sulphuric acid (5 c.c.) were heated in the water-bath for 10 minutes. The reaction mixtures were cooled, stirred into water (50 c.c.), neutralised with sodium hydroxide (2N), and extracted with ether. Both extracts yielded bright red solids (0·045 g.), each with m. p. 201—202° (decomp.). In solubilities and colours with dilute acids these solids were identical with *p'*-dimethylamino-*p*-hydroxyazobenzene, m. p. 201—202° (decomp.). The identity of the materials was confirmed by mixed melting point determinations.

Reduction. The substances (0·05 g.) were suspended in ethanol (5 c.c.), and 25% aqueous sodium hydroxide (10 c.c.) was added. An excess of zinc dust was added during 10 minutes with vigorous stirring. The reaction mixtures were diluted with water (100 c.c.) and extracted with light petroleum. Chromatography of each extract on alumina with light petroleum gave bright orange crystalline substances (0·02 g.), each with m. p. 115—117°. In chromatographic behaviour, solubilities, and colours with dilute hydrochloric acid these substances were identical with *p*-dimethylaminoazobenzene, m. p. 117·5—117·8°. The identity of the materials was confirmed by mixed melting point determinations.

Effect of heat. After being heated in sealed tubes at 200° for 1 hour both compounds were largely unchanged. Only the α-isomer showed slight decomposition.

Reactions of N-*Phenylhydroxylamine with Dimethyl*-p-*nitrosoaniline.*—The nitroso- and hydroxylamine compounds were of the same grade as those used for the preparation of the azoxy-compounds. The *N*-phenylhydroxylamine contained 6—10% of azoxybenzene. Treat-

ment of *N*-phenylhydroxylamine under the conditions used in the reactions below with the omission of the nitroso-compound gave azoxybenzene and azobenzene in quantities similar to those obtained in the reactions themselves. The various substances described were identified by their chromatographic behaviour, colour reactions with dilute hydrochloric acid, and mixed melting points with authentic compounds. Attention should be drawn to variations in the appearances of the materials on different batches of alumina. For example, the symmetrical azoxy-compound described was scarlet on some batches and a dull orange on others.

Reaction in presence of alkali. Solutions of the hydroxylamine (5 g. in 30 c.c.) and the nitroso-compound (5 g. in 60 c.c.) in ethanol were mixed and a few drops of 1 : 1 aqueous potassium hydroxide added immediately, with shaking. The reaction was then conducted as in the preparation of the azoxy-compounds. In the chromatography all the solvent which passed through before the elution of the main orange zones was collected. Removal of the solvent from this fraction and rechromatography of the material in light petroleum gave rise to a small, rapidly eluted, pale orange zone which yielded a few mg. of azobenzene. Further washing of this column, now colourless, with light petroleum gave an eluate which yielded pure azoxybenzene (1·5 g.) From the main column the two broad orange zones were eluted as before, to give β- (0·6 g.) and α-*p*-dimethylaminoazoxybenzene (0·8 g.). These two orange zones were followed by a third orange zone and then a scarlet zone. The alumina was pushed out and the region containing these two zones was cut off, made into a small column, and washed clear with hot benzene. Rechromatography on a small column with benzene effected a separation. The orange zone gave impure material (0·005 g.), m. p. 250—265°; this may have been *pp'*-bisdimethylaminoazobenzene, m. p. 266°. The scarlet zone yielded *pp'*-bisdimethylaminoazoxybenzene (0·05 g.).

Reaction without alkali. A solution of the nitroso-compound (5 g.) in ethanol (60 c.c.) was cooled in ice. The hydroxylamine (5 g.) was added and the mixture kept at room temperature for 30 minutes, and then refluxed for 1·75 hours. The alcohol was removed by distillation and the residue taken up in 1 : 4 benzene–light petroleum. This was chromatographed on an alumina column (8 × 1·25″). The chromatography conducted as above gave a trace of azobenzene, azoxybenzene (2·2 g.), *p*-dimethylaminoazobenzene (0·037) g.), β- (0·045 g.) and α-*p*-dimethylaminoazoxybenzene (0·15 g.). Zones were present corresponding to the symmetrical azo- and azoxy-compounds but separations of these were not effected.

Decomposition of Nitrosobenzene.—Nitrosobenzene (2 g.), purified by steam distillation, was suspended in dry ethanol (20 c.c.), and the mixture refluxed for 1·75 hours. The ethanol was removed by distillation and the residue extracted with cold light petroleum (3 × 30 c.c.). The extract was poured on to an alumina column. This was washed with light petroleum and the colourless eluate collected in fractions until a fraction devoid of dissolved material was obtained. Pure azoxybenzene (0·3 g.) was recovered from the various fractions. It was identified by direct comparison with a known sample of the substance. No azoxybenzene was detected in an untreated sample of the nitrosobenzene.

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Research Department, Glasgow Royal Cancer Hospital.

[Present Address: Physics Department,
Royal Cancer Hospital, London.]

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320. *Hysteresis in the Transitions in Ammonium Chloride, Hexamminonickel Nitrate, Silver Mercuri-iodide, Hexachloroethane, and Carbon Tetrabromide.*

By D. G. Thomas, L. A. K. Staveley, and (Miss) A. F. Cullis.

Dilatometric investigations are described on transitions in the substances named in the title. The primary object of these studies was to obtain further evidence bearing on a recently proposed theory of hysteresis. The basis of this theory, that the hysteresis is confined to the almost isothermal part of a transition, was confirmed.

It was found that the presence of solvents, so far from eliminating the hysteresis displayed by ammonium chloride, in fact may widen the hysteresis loop. Unusual behaviour was observed with hexamminonickel nitrate in that the transition region moved several degrees as the sample aged; also for this substance and for silver mercuri-iodide the hysteresis effects depended somewhat on the thermal history of the sample. For the first-order transitions in carbon tetrabromide and hexachloroethane the true equilibrium transition temperatures T_e were established, and here hysteresis was confined to cooling. Also for these transitions, once the change set in, it proceeded to completion, except at T_e.

Some measurements were made on the rates of volume change in the transition regions. Different types of behaviour were observed and it seems that for some transitions, *e.g.*, that in ammonium chloride, the overall rate of change is controlled by the rate of formation of self-propagating nuclei, whereas for others, *e.g.*, that in hexachloroethane, both this and also the rate of subsequent growth from these nuclei determine the overall rate.

In a previous paper (Thomas and Staveley, *J.*, 1951, 2572, which we shall refer to as Part I), it was suggested that hysteresis in solid–solid phase transitions arises simply from the difficulty of the initial formation of a new phase within an old. It was pointed out that hysteresis should only arise when part at least of the transition occurs isothermally and that the hysteresis should be associated with this part; also that the transition should proceed at all temperatures except at an equilibrium temperature, T_e, providing (i) that both forms are present in bulk and in an unstrained condition, and (ii) that there is a genuine dynamic equilibrium between the two forms. In addition it was thought that, though the established instances of hysteresis were confined to co-operative changes, the phenomenon should appear in normal first-order changes as well. This paper describes some experiments on the transitions in ammonium chloride, hexamminonickel nitrate, silver mercuri-iodide, hexachloroethane, and carbon tetrabromide, which were designed to test these predictions.

The λ-point in ammonium chloride was studied in the presence of solvents in an attempt to bring about a dynamic equilibrium between the two forms. We have also investigated whether the transition characteristics are altered if the substance is in contact with liquids of different kinds in which it is insoluble. The transitions in hexamminonickel nitrate and silver mercuri-iodide begin gradually but end almost abruptly, and so should provide further examples of the association of hysteresis only with the nearly isothermal part of the change. Hexachloroethane and carbon tetrabromide have transitions which occur apparently entirely isothermally, and according to our views these should therefore show hysteresis.

Experimental

Preparation of Materials.—Ammonium chloride. "AnalaR" ammonium chloride was purified by a single sublimation in a vacuum.

Hexamminonickel nitrate. A solution of nickel nitrate was obtained by adding an excess of nickel oxide to nitric acid; the oxide was prepared by decomposing the oxalate, which had been precipitated from hot solutions of "AnalaR" nickel chloride and oxalic acid, at 400—500°. Ammonia solution (*d* 0·88) was added dropwise to the cooled nitrate solution, precipitating the

complex (King, *J.*, 1932, 2928). The crystals were washed with ammoniacal alcohol and ether and kept in a desiccator over soda-lime in an atmosphere of ammonia, at first at 0°. After about 4½ months a sample was removed from the desiccator and analysed for ammonia volumetrically, and for nickel by means of dimethylglyoxime [Found : NH_3, 35·6; Ni, 20·66. Calc. for $Ni(NH_3)_6(NO_3)_2$: NH_3, 35·87; Ni, 20·60%].

Hexachloroethane. 1 Kg. of technical hexachloroethane was crystallised from alcohol, and 720 g. of the product were then subjected to three fractional sublimations at 70° at a pressure of 1 mm. or less. 243 g. were finally collected. There was no appreciable improvement in the purity after the second and third sublimations.

The constancy of the triple point was used as a criterion of purity. The sample was sealed under vacuum in a glass tube with a re-entrant thermocouple well. No stirring was possible. Heating and cooling curves were taken, and in this simple apparatus the final specimen melted over a range of 0·1°.

Silver mercuri-iodide. This was prepared by adding silver nitrate (in the dark, with mechanical stirring) to a solution of mercuric iodide in the minimum amount of potassium iodide. Three samples, A, B, and C, were made and studied dilatometrically. In the preparation of A and B, only about three-quarters of the stoicheiometric amount of silver nitrate was added, to avoid the formation of a product containing free silver iodide (cf. Ketelaar, *Z. Krist.*, 1931, **80**, 190). The results obtained with A and B suggested that each of these samples consisted of two solid phases; this was supported by a microscopic examination, which showed both to be a mixture of orange and yellow crystals. Accordingly, in preparing C, exactly stoicheiometric quantities were used, and this, under a microscope, appeared to consist solely of yellow crystals.

In the preparation of sample A, the silver nitrate was added very slowly to a hot solution of mercuric iodide in potassium iodide, in the hope of producing relatively large crystals, but B was made by rapid mixing of the cold reagents with the object of producing small particles. These were probably smaller than those composing A, since they settled more slowly. There were no obvious differences between *X*-ray powder photographs of A, B, and C.

Dilatometers.—The dilatometers were filled with the substance under investigation and then evacuated, if necessary with cooling in solid carbon dioxide, and sealed off. The liquid was usually introduced by breaking open the tip at the top of the capillary of the dilatometer under the surface of the liquid, previously degassed, and any excess of liquid then removed by evaporation. Sometimes the filling was accomplished by distillation. About 20 g. of ammonium chloride were used in each dilatometer with 1 mm. diameter capillaries; similarly about 10 g. of hexamminonickel nitrate and about 40 g. of hexachloroethane were used with capillaries of about 1·3 and 1·4 mm. diameter, respectively.

For carbon tetrabromide considerable difficulty was experienced in finding a suitable confining fluid necessary for a dilatometric investigation. Water was known slowly to hydrolyse the substance. With mercury, dilatometric readings were not reproducible, perhaps partly because mercury does not wet this solid and so cannot penetrate crevices, and partly because of its inability to dissolve occluded gas which is released when crystals break up. Finally, perfluoromethyl*cyclo*hexane was chosen as it was believed that carbon tetrabromide should have a relatively low solubility in this liquid (cf. Hildebrand, Fisher, and Benesi, *J. Amer. Chem. Soc.*, 1950, **72**, 4348), an expectation substantiated by our observations.

Thermostats.—All volume measurements were made at constant temperature. For the examination of ammonium chloride and hexamminonickel nitrate the thermostat, constant to within ±0·002°, previously described (Thomas and Staveley, *J.*, 1951, 1420) was used. For hexachloroethane, where temperatures were required near 40°, the same thermostat was used, but now the vapour-pressure regulator was filled with carbon disulphide in place of methyl chloride; this meant that the external tubes had to be electrically heated, and that thermostated water at about 50° had to be circulated around the mercury column. In addition the temperature was now measured with a platinum-resistance thermometer.

For carbon tetrabromide and silver mercuri-iodide again a Dewar vessel was used as a thermostat, temperature control to within ±0·01° being effected by a toluene regulator with a Sunvic proportionating head. The temperature was measured with a platinum resistance thermometer, or with mercury thermometers calibrated against this.

Results.—Ammonium chloride. Seven similar dilatometers were filled from the same batch of ammonium chloride; each was then filled with a different liquid and all were studied in the same thermostat simultaneously. A second batch of crystals was made and this was used to fill three dilatometers. The results were plotted as dilatometer readings against temperature and are not reproduced. The absolute volume changes were not calculated. For each dilato-

meter 44 readings were obtained with two runs for ascending, and three for descending temperatures. The results were quite reproducible except that on the first descending run, before which the samples had only been through the transition once, T_c occurred 0·06—0·07° below the temperature which was finally adopted after the transition had been traversed several times (T_c and T_w are the temperatures at which dV/dT is maximum for cooling and warming runs respectively). This contraction of the loop to a constant width as the sample is repeatedly subjected to the change has been reported previously for other substances (Smits, Tollenaar, and Kröger, *Z. physikal. Chem.*, 1938, *B*, **41**, 215) but not so far for ammonium chloride: it may be connected with the break up of the crystals due to the volume change.

Each limb of the hysteresis loops covered 0·1°; this diffuseness is almost certainly derived from the lack of careful purification, for previous experiments have shown that the transition can be much sharper (Thomas and Staveley, *loc. cit.*, p. 1420). Nevertheless, it was easy to detect differences in the behaviour of different samples. The table summarizes the results of these experiments, and those of previous investigations are included for comparison. For batch no. 2 the saturated solutions of the ammonium chloride in the alcohol–water mixtures at the temperature of the transition were very roughly 1·2N and 0·6N for the 50% water and 25% water mixtures respectively.

Transition characteristics for ammonium chloride as obtained by different authors using different dilatometric fluids.

Batch no. or ref.*	Composition of surrounding fluid	T_w	T_c	Width of loop, ΔT
1	CS_2, $CHCl_3$, $COMe_2$, n-C_7H_{16}, MeOH, 90% MeOH + 10% H_2O (by wt.)	−30·59°	−30·88°	0·29°
	39% MeOH + 61% H_2O	−30·55	−30·93	0·38
2	CS_2	−30·60	−30·86	0·26
	~75% MeOH + 25% H_2O	−30·615	−30·91	0·295
	~50% MeOH + 50% H_2O	−30·555	−30·955	0·40
a	Cymene	−30·52	−30·79	0·27
b	CS_2 (large crystals)	−30·55	−30·90	0·35
	CS_2 (small crystals)	−30·61	−30·86	0·25

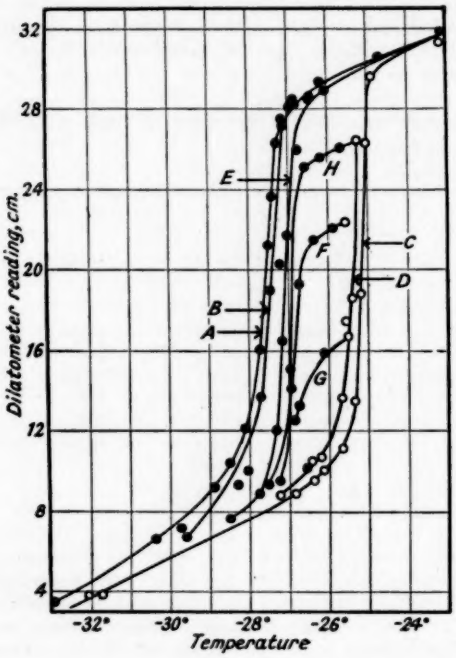
* (*a*) Smits and MacGillavry, *Z. physikal. Chem.*, 1933, *A*, **166**, 97.
(*b*) Thomas and Staveley, *loc. cit.*, p. 1420.

It can be seen that from one batch of crystals to another there are significant differences in the widths of the hysteresis loops, and also in the values of T_w and T_c. These differences can probably be ascribed to differences in crystal size, the nature of the surfaces, and so forth. However, for one batch of crystals there is no detectable difference in the hysteresis characteristics in the presence of any of the liquids tried, except for the water-rich methyl alcohol–water mixtures when the loop is definitely broadened, *e.g.*, from 0·29° to 0·38°. Despite the considerable solubility of the salt in these mixtures the volume still reached a steady value both on the limbs of the loop and within it, in the usual time of 2—3 hours. Thus, if, as we have supposed, at intermediate points on the limbs two phases exist side by side, in this instance the solvent does not set up rapid equilibrium between them. On the contrary, in broadening the loop it would appear to hinder nucleation. How it does this is not clear. The effect may be due to the influence of the dynamic equilibrium on the surface irregularities, or since water–alcohol mixtures are capable of strong interaction with ions, it may be connected with the forces between the surface and the liquid which will, in principle, affect free-energy relationships in the system as whole.

A number of observations were made on the rate of attainment of equilibrium. These showed that there was always a continuous decrease of the velocity of the transition as the change proceeded. By the time temperature equilibrium had been reached a considerable proportion of the change was over, but the following two examples show that the maximum velocity occurred, if not at zero time, at least well before a half or even a third of the volume change had been recorded. In going from −30·885° to −30·915° the meniscus in the dilatometer containing ammonium chloride and acetone fell by 3·04 cm. in 3 hours and was still falling after this time. No measurements were made in the first half hour, during which the meniscus fell

by 1·08 cm., but from the end of this period onwards the velocity fell continuously. Similarly in going from −30·915° to −30·953° the fall in the dilatometer containing ammonium chloride and 39% methyl alcohol and 61% water, over 140 minutes was 3·48 cm., of which only 0·98 cm. occurred in the first 20 minutes, yet after this period the rate was already diminishing.

Hexamminonickel nitrate. A calorimetric study of this salt (Long and Toettcher, *J. Amer. Chem. Soc.*, 1942, **64**, 629) has revealed a gradual transition from 173° to 247° K, with a maximum value of dC_p/dT at 243·3° K (−29·9° C). The change is associated with the disordering of the orientation of the nitrate ions. It also seemed likely from rough cooling curves that the transition exhibited hysteresis. Since a thermostat for this temperature region was available it was decided to investigate the change dilatometrically. It was found that hysteresis was associated with the final part of the change which occurred almost isothermally, and the general behaviour was similar to that of ammonium chloride. But a number of unusual observations



Plot of dilatometer readings against temperature in the region of transition in hexamminonickel nitrate (fourth sample). Open circles warming, full circles cooling.

were made on the dependence of the transition characteristics on the age of the sample and on its thermal history.

Four samples of the substance were investigated, all taken from the same material; this had been kept in a desiccator at 0° over soda-lime in an atmosphere of ammonia for a week, after which the first sample was removed. Subsequently it was kept in the same desiccator with ammonia but at room temperature. The salt has a considerable vapour pressure of ammonia at room temperature and will decompose if left in the open, but under the conditions employed this decomposition appeared to be avoided, as was indicated by the analysis made 4 months after the preparation.

The first runs on the first sample confirmed the presence of a transition with hysteresis, but no part of the change was at all sharp, the limbs of the loop stretching over 4°. However, as the change was repeated it became sharper, and the loop rather narrower. Also it was found that for descending temperatures T_c depended somewhat upon the temperature from which the sample had been cooled. Very roughly for this sample T_w was −30·6°, and T_c was −33·1°.

The second sample was taken from the desiccator 23 days after its preparation. It had a fairly sharp transition, and again the descending limit of the loop depended on the temperature from which cooling occurred, though a limiting value was reached when it was cooled from well

above the transition. However, T_w was −27·1° and T_c was −29·7°, a rise of no less than 3·5° and 3·4° respectively over the values for the first sample.

The third sample, removed after 34 days in the desiccator, behaved similarly except that there was a further rise in T_w and T_c, which were now −26·0° and −28·3°, respectively.

The fourth sample, removed after 120 days, was more carefully examined than any of the others. Capillary readings are plotted against temperature in the figure. The limbs of the hysteresis loop are seen to be not far from vertical, covering 0·1—0·5°. The contraction in the loop as the transition is repeated is illustrated by curves *A* and *B*, and *C* and *D*, *B* and *D* occurring after *A* and *C*: here the contraction is 0·1—0·3°. *A* and *B* were obtained by cooling the specimen from room temperature. Curves *H*, *F*, and *G* show what happens if the system is cooled from the limb for ascending temperatures: it appears that a limiting downward limb is followed at about −26·9°, whereas curve *B* from room temperature lies at about −27·4° (T_c). If the system is cooled from just above the transition, *e.g.*, from −23·15° (after being warmed from −78°), the intermediary curve *E* is followed. It would seem that there is a family of curves that can be followed falling between *H*, etc., and *B* depending upon the starting point. No such effect occurs for warming: curve *D* has on it points representing the system when it had been warmed from −78°, and from −27·5° (reached by following a curve such as *F*) just below the transition. This is further confirmed by the fact that on warming from one of the downward curves the ascending limiting curve is regained, as previous experiments on the other samples had shown. T_w for this transition is about −25·3°. These effects may be connected with the growth of the crystallites and the gradual elimination of their imperfections which would affect the transition characteristics: it is conceivable that the effect is more marked for cooling than for warming because the disordered regions above the transition may more readily fuse together than the ordered regions, existing below the transition, which will have their symmetry axes randomly directed. Possibly the preservation in crevices of nuclei may also play a part (Turnbull, *J. Chem. Phys.*, 1950, **18**, 198).

It can be seen that from the first to the last specimen the mean temperature of the transition rose by about 5·5°; in the last specimen the loop was about 2·1° wide. Since the fourth sample had a higher transition temperature than the third, there is no reason to suppose that the fourth represents the limit: T_w for the fourth sample is 4·6° higher than that reported by Long and Toettcher (*loc. cit.*). Once the specimens are in the dilatometers and surrounded by carbon disulphide, the transition characteristics remain approximately the same. This would indicate that whatever change was occurring to alter the transition temperature, took place in the desiccator. Thus this process might have been drying or possibly a gradual perfection of the crystals by the dynamic equilibrium of ammonia set up between the solid and the gas phase, though neither suggestion seems convincing. Indeed, it is hard to see that impurities, etc., should be the cause of the effect, for the sharpness ultimately obtained of the final part of the transitions did not alter markedly from one sample to the next. The analysis, carried out 15 days after the fourth sample had been removed, was satisfactory (see above).

The kinetic behaviour resembles that of ammonium chloride. Away from the immediate vicinity of the hysteresis loop, equilibrium is attained at once, but on the limbs of the loop several hours elapse before the meniscus becomes constant, yet the velocity of the change is always observed to decrease as the change proceeds, and has certainly reached a maximum before 50% of the change has occurred. Thus, on cooling of the fourth sample from −26·734° to −26·995° an alteration in dilatometer reading of 6·5 cm. during 2 hours took place and the volume was still changing very slowly at the end of this time, but 3 cm. of this change occurred in less than the first 20 minutes.

As discussed in Part I we believe that there is only one temperature T_e at which the high- and low-temperature forms can coexist in true equilibrium. An unsuccessful attempt was made to determine T_e for this system as follows. By alternately heating and cooling the sample five times over part of the transition region, and then plunging the dilatometer into the thermostat at −25·53°, the point falling at the highest temperature on curve *F* was obtained. Curve *F* was traced out on cooling from this temperature and was similar to curves *H* and *G*, where no attempt had been made to secure intimate mixing of the two forms.

Hexachloroethane. Hexachloroethane has two first-order transitions, one near 44°, and one near 71°; only the first of these was studied and the sample was never taken through the high-temperature change. Previous work had shown that hysteresis of a kind occurred at both transitions, though it was thought that it was different from that typified by ammonium chloride because T_e could be definitely established, and only at this temperature did the two forms coexist in equilibrium (Wiebenga. *Z. anorg. Chem.*, 1935, **225**, 38). Nevertheless, supercooling

occurred at both transitions, but the evidence left the question of superheating open, though if superheating occurred at all it was less than the supercooling.

The system behaved very differently from those previously investigated; once the transition had begun either on cooling or warming it always proceeded to completion, the rate beginning slowly, rising to a maximum usually at about 50% conversion, and then declining. Rate measurements were made at different temperatures for ascending and descending runs, and these rates, measured both by the maximum value achieved and the time taken to reach this maximum value, varied very rapidly with temperature (cf. Hartshorne, *Discuss. Faraday Soc.*, "Crystal Growth," **1949**, **5**, 149). The rates also depend on the temperature from which heating or cooling had taken place.

Wiebenga found the true equilibrium temperature for the transition to be 43·6°, by arranging that both forms should be simultaneously present by previously heating and cooling the sample partially through the transition, and then observing the temperature at which the meniscus was steady. We similarly found T_e to be 44° ± 0·1°. The highest temperature at which the transition was observed to commence on cooling was 41·00°; at 42·44° the specimen remained in the high-temperature form for 5 days without sign of change (though if both forms were present at this temperature the transition proceeded comparatively rapidly). This showed that the change could be supercooled by several degrees. Measurements at 44·08° and 44·26°, lasting 4 or 5 days each, showed that at both these temperatures the change started spontaneously, although very slowly, without the introduction of the high-temperature form. Hence superheating of the transition is either non-existent or very small.

Carbon tetrabromide. The investigation of carbon tetrabromide was not as thorough as that of hexachloroethane, but the essential characteristics were revealed. Hysteresis of the order of 1° was definitely present: for ascending temperatures the system remained in the low-temperature form for at least 9 hours at 46·80°, but at 46·96° after 24 hours the change was about 85% finished, and was still occurring. For descending temperatures the system remained in the high-temperature form for 4 hours at 46·11° and showed no sign of changing, but at 45·98° the transition had taken place completely in about 12 hours. To find T_e, the same technique of "activation" was used as had been adopted for hexachloroethane, and showed that T_e lay above 46·78°, but below 46·88°. Thus, as before, superheating is absent or too small to be detected. As with hexachloroethane, it was not possible for the two forms to co-exist side by side in the dilatometer except at T_e; once the change had started it proceeded to completion.

The remarkable fact about this transition is that for *ascending* temperatures the rate of change is maximum at least as soon as measurements become possible and certainly well before half the change has taken place, just as for ammonium chloride, but for *descending* temperatures the change begins slowly, rises to a maximum when half the mass is transformed, and then declines again just as for hexachloroethane.

Silver mercuri-iodide. The existence of a transition in this substance, accompanied by a colour change, has long been known. Ketelaar (*loc. cit.*; *Z. physikal. Chem.*, **1934**, *B*, **26**, **327**; **1935**, **30**, 53) has shown that it is partly gradual and partly sharp, and has elucidated the ionic redistribution which it involves. The accompanying volume change is relatively small, and in the transition region equilibrium is attained very slowly. These factors make a precise dilatometric study rather difficult. Nevertheless, our investigations revealed some interesting features.

All three samples of this substance appeared to undergo two transitions, the first reaching completion between 46° and 47°, the second at 51°. Both transitions displayed hysteresis. We consider, however, that pure silver mercuri-iodide has only one transition, namely, that culminating at ~51°, not only because this agrees with the temperature recorded by Ketelaar, but also because with the third sample C, the lower transition was much less pronounced. In the light of these facts, together with the results of the microscopic examination and the phase-rule study of the silver iodide–mercuric iodide system carried out by Steger (*Z. physikal. Chem.*, **1903**, **43**, 595), it is probable that our samples were mixtures of two phases, one being the pure substance, and the other a solid solution of mercuric iodide in silver mercuri-iodide.

We shall deal first with the transition in pure silver mercuri-iodide. We agree with Ketelaar that, while this begins gradually, the greater part of the change involved occurs almost isothermally. For samples A and B about half of the total volume change occurred between 50·7° and 50·8°, and for C, between 51·3° and 51·4°. The coefficient of expansion of the solid, however, did not revert to its normal low value until the temperature of 50·8° (for A and B), or 51·4° (for C), had been exceeded by several tenths of a degree. As was expected, the hysteresis, which amounted to ~4°, was confined to the discontinuous part of the change. For samples

A and B, for example, the volume–temperature curve for the gradual part of the transition (*i.e.*, up to ~50·7°) was exactly retraced on cooling from a maximum temperature not exceeding 50·7°. It was observed, however, that the cooling and warming curves did not differ very much even when the maximum temperature attained on warming was as high as 51·4°, and that the hysteresis was only fully developed when this maximum temperature was about 2° above that of the almost isothermal part of the transition. Similar results were obtained with sample C. With sample B (believed to consist of smaller crystals than the others), the cooling curves were more uniformly distributed across the hysteresis loop : some of the cooling curves for sample B were near the middle of the loop, whereas those for samples A and C were near one of the two boundary curves.

No attempt was made to assess T_c for this transition, but the results suggest that it is very close to T_w (*i.e.*, 50·7° for samples A and B). We have already noted that, on warming, the transition is not completed until the temperature is definitely above 50·7°, and it is therefore likely that if 51·0°, for example, is the maximum temperature reached, the majority of crystals still retain at this temperature nuclei or small regions wholly or partially in the low-temperature form. On cooling, these nuclei will induce reversion to the low-temperature form on reaching T_c, so that if this is very near 50·7°, the volume–temperature curve should revert to the warming curve. That such a cooling curve falls slightly above that for warming would then mean that at 51·0° all traces of the low-temperature form have disappeared from a few crystals, and that for these, nucleation will not set in on cooling until the temperature is 3—4° below T_c. Since the proportion of such crystals at a given maximum temperature should, *ceteris paribus*, be greater for smaller than for larger crystals, we can understand why the cooling curve for the former is found to lie further away from the warming curve. But for small or large crystals the full hysteresis effect will only appear when the substance has been heated to a sufficiently high temperature for all vestiges of the low-temperature form to have vanished. For samples A and B, this temperature is about 52·5°. Our observations on this transition indicate that, unlike that in ammonium chloride, it is not a change which proceeds rapidly throughout a crystal unit once nucleation has set in. It would, in fact, be expected that the ionic migration involved would have a considerable activation energy.

The lower transition, which we believe to be associated with a mixed-crystal phase, was not investigated so thoroughly. This transition was, however, found to present a rather striking example of a phenomenon to which we have called attention elsewhere (p. 1731), namely, the dependence of T_c (the temperature at which the cooling curve rejoins the warming curve) on $T_{max.}$, the highest temperature reached, *i.e.*, the dependence of the width of the hysteresis loop on the thermal history of the substance. This is shown by the following figures :

$T_{max.}$	48·0°	49·3°	52·2°	70·6°
T	42·8	41·8	40·7	27·0

Discussion

A complete treatment of the results we have presented would require consideration both of the factors affecting the rate of nucleation and of those determining the subsequent growth rate of a phase from a nucleus. It is not easy, and perhaps not justifiable, to attempt to separate these two processes from each other. It will, however, be convenient to consider first these results in the light of the theory relating hysteresis with nucleation (Part I).

The fundamental idea on which the theory was based is upheld, namely, that hysteresis is confined to the almost isothermal part of a transition, and conversely that any change which is partly or wholly isothermal displays hysteresis. The question arises, however, whether it is correct to identify the hysteresis exemplified by that at the λ-point in ammonium chloride (where it is possible to stop at any point on the limbs of, or within, the loop), with that associated with a completely first-order transition such as that in hexachloroethane (where the two forms can only coexist at one temperature). Smits and his school (*e.g.*, Wiebenga, *loc. cit.*) considered that the two kinds of hysteresis are fundamentally different. We believe, however, that the basic reason for hysteresis existing at all is universal, namely, the difficulty of the appearance of a new phase within an old. We suggest that what determines whether hysteresis at a transition resembles that in ammonium chloride on the one hand, or that in hexachlorethane on the other, is whether or not a crystal unit in one

form can affect neighbouring units in the other form in which nuclei have not yet appeared. As discussed in Part I, the phenomena within the hysteresis loop for ammonium chloride and hexamminonickel nitrate are comprehensible if we suppose that the crystal units are quite independent of one another. (Here we may recall that for ammonium chloride even solvent does not establish equilibrium.) By contrast, for hexachloroethane, since once the change has started it proceeds throughout the whole crystal mass, and since in our experiments the two forms can only coexist at one temperature, we must conclude that contact between adjacent units in the two forms in these circumstances can bring about transformation of the less stable. With silver mercuri-iodide it seems that growth from nuclei is slow so that it can proceed part of the way in any one crystal unit and then be reversed; but that again there is no interaction between different crystal units. The apparent lack of mutual interaction for ionic solids may perhaps be connected with their hardness and involatility. Furthermore, when a form of one density grows within another, it may happen that the strains set up result, with a comparatively incompressible ionic crystal, in its fracture into very small units which may be further subdivided when subjected to the transition again. (This may be connected with the observations to which we have already drawn attention—that hysteresis loops can contract on repeated passage through the transition until a limiting state is reached.) In molecular crystals it is possible that their greater compressibility renders them less prone to disruption through internal strain, so that the crystal unit which can be changed by one nucleus may be much larger, and further that the greater volatility of such substances may make possible molecular movement across narrow gaps between crystals of the two forms.

We have already observed that with carbon tetrabromide and hexachloroethane the hysteresis is confined to the supercooling. It is impossible to say whether the same is true for ammonium chloride and hexamminonickel nitrate since we have been unable to establish T_t for these transitions. That superheating, however, is sometimes possible in first-order phase change has been demonstrated, *e.g.*, by Meerman for 1 : 2-dibromoethane (*Rec. Trav. chim.*, **1942**, **61**, 860). In the nucleation theory of hysteresis under discussion, nucleation was assumed to start in crystals from within; if this is so both for heating and for cooling, the theory would require hysteresis in both directions. It was, however, pointed out that if energetic relationships are such that in one direction, for example on heating, nuclei start on the surface, then it could happen that there would be no, or at least much reduced, hysteresis on warming, though it would then seem inevitable that on cooling, nucleation would begin within the crystals and that there would be supercooling. We may mention that although it is normally impossible to superheat a solid above its melting point, Haykin and Bénet (*Compt. rend. Acad. Sci. U.R.S.S.*, **1939**, **23**, 31) have shown that for tin, provided superficial melting is prevented, the solid can be superheated by at least 2°.

Our observations on the *kinetics* of the transitions may be summarized as follows. For ammonium chloride and hexamminonickel nitrate, on alteration of the temperature in the region of the almost isothermal parts of the transitions, by the time temperature equilibrium has been obtained and quantitative measurements of the rate become possible, this rate is found to decrease continuously as the change proceeds. Admittedly, by the time measurements can be made nearly half the change may be over, but there is no doubt that the rate is maximum at or near the start of the transition.

For hexachloroethane, as mentioned above, the behaviour was quite different. The rate of change always passed through a maximum at approximately 50% conversion, and the change once started always led to *complete* conversion of the whole sample from one form into the other.

With carbon tetrabromide the behaviour was again different. Whereas the rate of formation of the low- from the high-temperature form passed through a maximum at about 50% conversion as for hexachloroethane, yet the rate of the reverse change apparently decreased continuously with time and so must have had its maximum at or near the start of the transition. In this latter respect it therefore resembles ammonium chloride except that once the change has begun it leads eventually to complete conversion.

It seems to us that many more results of the kinetics of transitions are needed before

generalizations can safely be made and before all the factors involved can be fully understood. The rate at which a transition takes place without artificial inoculation or "seeding" must in principle be dependent both on the rate of production of nuclei and on that of subsequent growth. It may be that in some systems one of these two factors predominates. Thus the rate of nucleation may be slow relatively to that of subsequent growth, and so rate-determining. If the crystal mass consists of a large number of independent particles then the rate of nucleation will be proportional to the amount of unchanged material so that, if we assume that subsequent growth is very rapid, the overall observed rate, reflecting exactly the nucleation rate, will decline with time, resembling that of radioactive decay. This may be the state of affairs for ammonium chloride and hexamminonickel nitrate. It is not unreasonable for the transitions in these substances that the changes emanating from nuclei should proceed rapidly since they only involve ionic reorientation, in contrast to the transition in, say, hexachloroethane where there is a deep-seated structural change. There is, in addition, a secondary factor which will also operate to give a steadily declining rate as the transition proceeds, namely, the fact that different crystal units are almost certainly not identical. Evidence has already been presented (Thomas and Staveley, *J.*, 1951, 1420) that factors such as particle size, impurities, and so on can affect the transition characteristics and hence must modify nucleation rates. It is this factor which must make it possible for the system to reach apparent equilibrium on the nearly vertical limbs of the hysteresis loop.

On the other hand, subsequent growth may also be slow. If this rate depends upon the area of the interphase boundary, which is probably often true, we should expect a maximum in the rate of about 50% change, as indeed we find for the transition in hexachloroethane where there is a radical crystal change, the development of which may be far from rapid. In general, if neither the rate of nucleation nor subsequent growth predominates, a combination of the two could lead to a maximum in the rate somewhere between zero and 50% conversion, and if it happens to fall near the start of the transition it may be difficult to establish its existence experimentally.

A further complication is that, as already indicated, nuclei may sometimes appear on surfaces, and the interphase area would reach a maximum before half the transformation is complete. Thus even if the observed rate of change is controlled by the rate of growth from nuclei and hence by the interphase area, its maximum would fall before 50% conversion. Although we do not fully understand why on warming of carbon tetrabromide the rate of conversion shows no observable maximum (in contrast to the behaviour on cooling and to that displayed by hexachloroethane), we think that it might be explained in terms of suitable relationship between nucleation rate and rate of subsequent growth, and that in addition surface nucleation may play an important role. We have already pointed out that the temperature at which the transition proceeds on warming is very near T_e so that the relationship between nucleation and growth rates may well be different from that prevailing in the region where the transition sets in on cooling. It must, however, be admitted that T_w is likewise very near T_e for the transition in hexachloroethane although here the rate of production of the high-temperature form shows a maximum.

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, November 20th*, 1951.]

321. *The Adsorption Method of Measuring Surface Areas.*

By R. M. Barrer, N. Mackenzie, and D. Macleod.

In order to investigate the accuracy of the adsorption method of measuring surface areas, a group of Brunauer, Emmett, and Teller (B.E.T.)-type multilayer isotherms has been derived, and examined by use of experimental sorption data obtained on montmorillonite and attapulgite. In the isotherms, the volatility of sorbate molecules was assumed to increase the higher the layer in which they were situated. This has the effect of reducing the excessive sorption given at higher relative pressure by the original B.E.T. equation. A number of the isotherms were in good agreement with the experimental data, and the v_m values derived from each of the successful isotherms were in satisfactory agreement. It is suggested that the adsorption method can in this case be a good absolute measure of surface area. If, as is quite often true of the original B.E.T. or Huttig equations, the isotherm fit is not good, values of v_m are less consistent and it is then considered that surface areas as determined by the adsorption method may not be accurate.

The adsorption method is among the commonest of the means of measuring the surface areas of finely divided solids. Most recent users of the method have employed the B.E.T. procedure (Brunauer, Emmett, and Teller, *J. Amer. Chem. Soc.*, 1938, **60**, 309; Brunauer, "Physical Adsorption of Gases," Oxford Univ. Press, 1944, pp. 155 *et seq.*) and a lesser number the Harkins and Jura (*J. Chem. Phys.*, 1943, **11**, 430; 1944, **12**, 112) or the Huttig (Ross, *J. Phys. Coll. Chem.*, 1949, **53**, 383) procedure. Recently, B.E.T. and Huttig isotherms have been compared in suitability for surface-area determinations (Corrin, *ibid.*, 1951, **55**, 612). Molecular cross-sections in adsorbed films were determined by using a sample of titania of known area, determined by the Harkins and Jura calorimetric method (*J. Amer. Chem. Soc.*, 1944, **66**, 1362). It was then noted that the cross-sections differed to some extent for B.E.T. and Huttig isotherms. Conversely, if equal cross-sections are taken for any molecule (*e.g.*, nitrogen), then B.E.T. and Huttig linear plots may lead to appreciably different surface areas. Similar observations have been made in using porous glass as sorbent (Barrer and Barrie, in preparation).

These results raise the question of the absolute as distinct from the comparative accuracy of surface-area measurements through adsorption. We have approached this problem by developing a series of B.E.T.-type multilayer isotherms all of which have at least as reasonable a physical basis as the standard B.E.T. equation. We have then used these isotherms, together with the standard B.E.T. and Huttig equations, to measure the surface areas of attapulgite and montmorillonite. It appears that it is not enough to determine surface areas always by use of a single type of isotherm; one should employ a group of isotherms to check the areas obtained with each against those obtained with the others. This should give a better idea of the probable absolute accuracy of such determinations.

B.E.T.-type Multilayer Adsorption Isotherms.—A limitation of the B.E.T. isotherm lies in the omission of lateral interactions between sorbate molecules (Hill, *J. Chem. Phys.*, 1946, **14**, 263; 1947, **15**, 767). Similarly, Huttig's isotherm is thermodynamically consistent if the sorbate is considered as a succession of independent layers in a field of potential due to sorbent and to lateral sorbate–sorbate interactions. This time vertical sorbate–sorbate interactions must be omitted (Barrer, *J.*, 1951, 1874). A second limitation of both isotherms as usually employed is that all sorbate molecules in layers other than the first are assumed to have liquid-like evaporation–condensation properties. It is this assumption which we propose to modify for the B.E.T. isotherm by making molecules more and more volatile the higher the layer. This will have the effect of smoothing the otherwise "wavy" surface of the B.E.T. adsorbed film, for it will make it highly improbable that any one molecular column can appreciably exceed any other in length. It will also reduce the total sorption at higher relative pressures, so partially correcting for the excessive sorption predicted by the isotherm at such pressures.

TABLE 1. *Special cases of isotherm equation* (3).

Values of m in eqn. (2)	Liquid-like evaporation condensation properties shown by	Isotherm : $v/v_m =$	Designation	Characteristic linear plot
$m_1 = 1, m_2 = 2, m_3 = 3$, etc.	2nd layer	$\dfrac{Cxe^x(1+x)}{1+Cxe^x}$	A	$\dfrac{1}{Cv_m}+\dfrac{1}{v_m}xe^x=\dfrac{x}{v}e^x(1+x)$
	3rd layer	$\dfrac{2Cxe^{2x}(1+2x)}{1+2Cxe^{2x}}$	B	$\dfrac{1}{Cv_m}+\dfrac{2}{v_m}xe^{2x}=\dfrac{2x}{v}e^{2x}(1+2x)$
	$(i+1)$th layer	$\dfrac{iCxe^{ix}(1+ix)}{1+iCxe^{ix}}$	C	$\dfrac{1}{Cv_m}+\dfrac{i}{v_m}xe^{ix}=\dfrac{ix}{v}e^{ix}(1+ix)$
$m_1 = 2, m_2 = 3, m_4 = 4$, etc.	2nd layer	$\dfrac{2Cxe^{2x}}{1+C(e^{2x}-1)}$	D	$\dfrac{1}{v_m}e^{2x}=\dfrac{2x}{v}e^{2x}+\dfrac{1}{v_m}\cdot\dfrac{C-1}{C}$
	ith layer	$\dfrac{iCxe^{ix}}{1+C(e^{ix}-1)}$	E	$\dfrac{1}{v_m}e^{ix}=\dfrac{ix}{v}e^{ix}+\dfrac{1}{v_m}\cdot\dfrac{C-1}{C}$
$m_1 = m_2 = 1, m_3 = 2, m_4 = 3$, etc.	2nd and 3rd layers	$\dfrac{Cx\{1+x(2+x)e^x\}}{1+Cx(1+x)e^x}$	F	$\dfrac{1}{Cv_m}+\dfrac{1}{v_m}x(1+x)e^x=\dfrac{x}{v}\{1+x(2+x)e^x\}$
	$(i+2)$th layer	$\dfrac{iCx\{1+ix(2+ix)e^{ix}\}}{1+iCx(1+ix)e^{ix}}$	G	$\dfrac{1}{Cv_m}+\dfrac{1}{v_m}ix(1+ix)e^{ix}=\dfrac{ix}{v}\{1+ix(2+ix)e^{ix}\}$
$m_1 = 1, m_2 = m_3 = \ldots = m$	2nd layer	$\dfrac{Cx\left(1+\dfrac{2mx}{m-x}+\dfrac{mx^2}{(m-x)^2}\right)}{1+Cx+\dfrac{Cmx^2}{m-x}}$	H	$\dfrac{1}{Cv_m}+\dfrac{x}{v_m}\left(1+\dfrac{mx}{m-x}\right)=\dfrac{x}{v}\left(1+\dfrac{2mx}{m-x}+\dfrac{mx^2}{(m-x)^2}\right)$
	3rd and higher layers	$\dfrac{Cx\left(1+\dfrac{2mx}{1-x}+\dfrac{mx^2}{(1-x)^2}\right)}{1+Cx+\dfrac{Cmx^2}{1-x}}$	I	$\dfrac{1}{Cv_m}+\dfrac{x}{v_m}\left(1+\dfrac{mx}{1-x}\right)=\dfrac{x}{v}\left(1+\dfrac{2mx}{1-x}+\dfrac{mx^2}{(1-x)^2}\right)$
$m_1 = m_2 = m_3 = \ldots = m^{f(x)}$	2nd and all higher layers, but only as $x \longrightarrow 1$	$\dfrac{Cx}{\left(1-\dfrac{x}{m^{f(x)}}\right)\left(1-\dfrac{x}{m^{f(x)}}+Cx\right)}$	J	$\dfrac{1}{Cv_m}+\dfrac{xm^{f(x)}}{v_m(m^{f(x)}-x)}=\dfrac{xm^{2f(x)}}{v(m^{f(x)}-x)^2}$
$m_1 = 1, m_2 = m_3 = \ldots m^{f(x)}$	2nd layer; and then in all higher layers when $x \longrightarrow 1$	$\dfrac{Cx\left\{1+\dfrac{2x}{1-\frac{x}{m^{f(x)}}}+\dfrac{x^2}{m^{f(x)}\left(1-\frac{x}{m^{f(x)}}\right)^2}\right\}}{\left\{1+Cx+\dfrac{Cx^2}{1-\frac{x}{m^{f(x)}}}\right\}}$	K	$\dfrac{1}{Cv_m}+\dfrac{x}{v_m}\left(1+\dfrac{m^{f(x)}\cdot x}{m^{f(x)}-x}\right)=\dfrac{x}{v}\left(1+\dfrac{2m^{f(x)}\cdot x}{m^{f(x)}-x}+\dfrac{m^{f(x)}\cdot x^2}{(m^{f(x)}-x^2}\right)$

Hence, the modified isotherms will not rest upon any worse premises than does the original B.E.T. isotherm, and indeed in the above respect may be physically more realistic. If we consider equilibrium between the $(i-1)$th and ith layers, we have

$$a_i x S_{i-1} = b_i S_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where S_i, S_{i-1} denote respectively the fractions of the surface occupied by columns i and $(i-1)$ molecules long, $x = p/p_0$ is the relative pressure, and a_i and b are the velocity constants for condensation and evaporation respectively. We may introduce the idea of increasing volatility of sorbate as i increases through the set of relations

$$\left.\begin{aligned} b_1/a_1 &= C \\ b_2/m_1 a_2 = b_3/m_2 a_3 = \ldots\ldots &= b_i/m_{i-1} a_i = \ldots\ldots = g \end{aligned}\right\} \quad . \quad . \quad . \quad (2)$$

where m_1, m_2, ... m_{i-1} . . . are numbers integral or fractional, and g is a constant. If one endows *second*-layer molecules with the evaporation–condensation property of a liquid, $m_1 g = 1$; if the *third* layer, then $m_2 g = 1$, and so on (cf. Brunauer, *op. cit.*, p. 153). Then the general form of the isotherm can readily be derived (cf. Dole, *J. Chem. Phys.*, 1948, **16**, 25):

$$\frac{v}{v_m} = y \, \mathrm{d} \ln \left(1 + \frac{Cy}{m_1} + \frac{Cy^2}{m_1 m_2} + \ldots\ldots + \frac{Cy^i}{m_1 m_2 \ldots m_i} + \ldots\ldots\right) \quad . \quad . \quad (3)$$

where $y = x/g$ and v, v_m have their usual B.E.T. significance.

Possible particular cases are then obtained by summation of the series of equation (3), and are summarised, with the underlying assumptions, in Table 1. In the last column of this table are given the linear plots relevant to the different isotherms. One may note that isotherm *A* recalls the original Huttig isotherm in form. Also for small enough values of x all isotherms tend to follow Henry's law, as expected, while for large C and smaller x they approach Langmuir's isotherm. Isotherms *D*, *E*, *F*, and *G*, on expansion of the exponentials and omission of terms in x^2 and higher powers, all take the form of Huttig's isotherm.

For the equations *A* to *G*, numerical values of m_1, m_2, etc., are assigned as reasonable possibilities, but from *H* onwards particular values of m are not assigned. Isotherm *I*, which gives more sorption at higher relative pressures than does the B.E.T. equation, need not be considered further. Equation *H* is, however, important and useful, as will be seen later.

In the case of the isotherms *J* and *K* a new idea is introduced. As the film thickens and x approaches unity, all layers should tend to develop liquid-like properties. This is allowed for in a semi-empirical manner by replacing m by $m^{f(x)}$, where $f(x)$ is a function of x such that as $x \to 1$, $f(x) \to 0$ and so $m^{f(x)} \to 1$. Thus, if we wish to derive the isotherm corresponding to *H*, but with the above modification, we replace part of equation (2) by

$$\frac{b_2}{m_1^{f(x)} a_2} = \frac{b_3}{m_2^{f(x)} a_3} = \ldots\ldots = \frac{b_i}{m_{i-1}^{f(x)} a_i} = \ldots\ldots = g \, . \quad . \quad . \quad . \quad (2a)$$

and in the usual way derive the isotherm

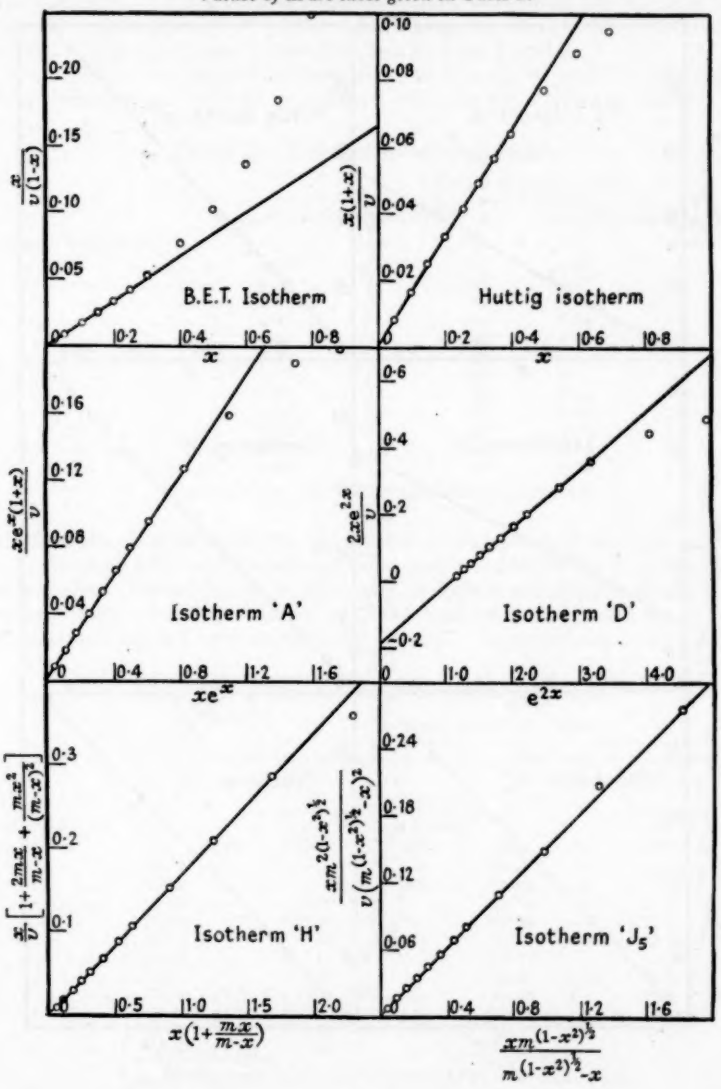
$$\left.\frac{v}{v_m} = \frac{Cx\left\{1 + \dfrac{2x}{1 - \dfrac{x}{m^{f(x)}}} + \dfrac{x^2}{m^{f(x)}\left(1 - \dfrac{x}{m^{f(x)}}\right)^2}\right\}}{\left\{1 + Cx + \dfrac{Cx^2}{\left(1 - \dfrac{x}{m^{f(x)}}\right)}\right\}}\right\} \quad . \quad . \quad . \quad . \quad (4)$$

Similarly, corresponding to the original B.E.T. isotherm one obtains

$$\frac{v}{v_m} = \frac{Cx}{\left(1 - \dfrac{x}{m^{f(x)}}\right)\left(1 - \dfrac{x}{m^{f(x)}} + Cx\right)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Suitable empirical functions $f(x)$ which have the requisite properties include: $(1 - x)$, $(1 - x)^{\frac{1}{2}}$, $(1 - x^2)$, $(1 - x^2)^{\frac{1}{2}}$, and so on. Equations *J* and *K* of Tables 2 and 3 exemplify these isotherm forms, and Figs. 3 and 4 illustrate their use.

FIG. 1. *Linear plots for comparison of theoretical isotherms. Nitrogen on montmorillonite at* 78° K. *Values of* m *are those given in Table 2.*

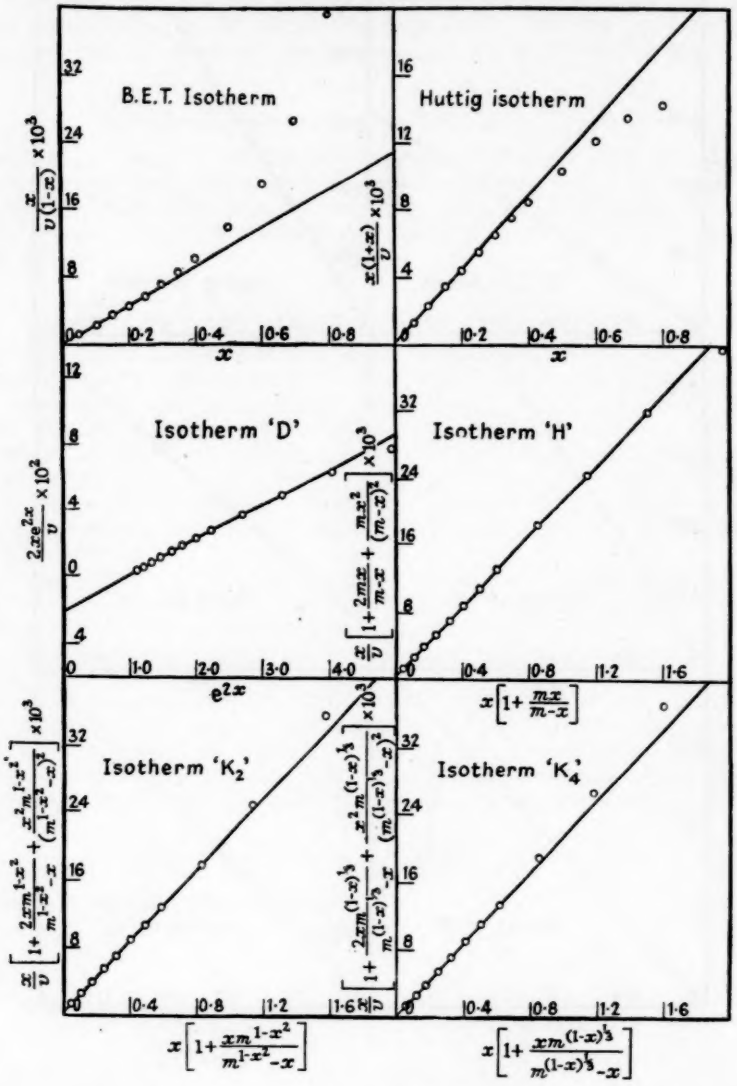


Applicability of the Isotherms: Surface Areas.—Sorption isotherms, which were of Type II in Brunauer's classification (*op. cit.*, p. 150), were measured for nitrogen at −195° on montmorillonite and attapulgite, and also for ammonia at −63·5° (the melting temperature of chloroform) on attapulgite. Isotherms on attapulgite showed little hysteresis; those on montmorillonite led at higher relative pressures to closed hysteresis loops. Where

hysteresis was obtained the equations of Table 1 were used to describe only the ascending part of the experimental isotherm.

Most of the theoretical isotherms, when applied to the experimental data after

FIG. 2. *Linear plots for comparison of theoretical isotherms. Nitrogen on attapulgite at* 78° K. *Relevant values of* m *appear in Table* 3.



rearrangement to the linear equations of column 5, Table 1, were found to give straight-line graphs over a considerable range in relative pressure. Examples of this behaviour are given in Figs. 1 and 2 which, for comparison, also show original B.E.T. and Huttig linear plots. The slopes of the linear part of such graphs in all cases give v_m, the amount of sorbate required to complete a monolayer of adsorbed gas. The intercepts, with v_m,

give the appropriate values of $C = \exp(-\Delta A_0/RT)$, where $\Delta A_0 \simeq \Delta G_0$ is the standard free energy of transfer from liquid sorbate to a Langmuir monolayer film (Barrer and Riley, *Trans. Faraday Soc.*, 1950, **46**, 853).

For the isotherms *H*, *J*, and *K* the correct value of m has also to be found. To do this, one uses the experimental isotherms to construct the linear graphs for the chosen theoretical isotherm. This is done for several values of m, until the value of m is found which gives the longest linear plot. This value is then the correct one. The corresponding longest straight lines are shown for several cases in Figs. 1 and 2.

One thus sees how the linear plots may serve to give v_m, m, and C. The values of the appropriate constants are collected in Tables 2 and 3 for the various isotherms. It should

TABLE 2. *Nitrogen on montmorillonite.*

	Values of constants *					
	Sorbent outgassed at 523° K :			Sorbent outgassed at 323° K :		
Isotherm designation	v_m	m	C	v_m	m	C
B.E.T.	5·73	—	500	4·38	—	761
Huttig	5·98	—	310	4·77	—	131
A	6·25	—	80	5·05	—	49
B	4·98	—	−ve	3·84	—	153
D	6·00	—	100	4·62	—	26
F	7·69	—	30	6·02	—	30
H	5·79	1·4	600	4·61	1·5	100
J_1, $f(x) = 1 - x$	7·27	5·0	68	5·89	5·0	42
J_2, $f(x) = 1 - x^2$	7·44	3·0	122	6·25	3·0	24
J_3, $f(x) = (1-x)^{\frac{1}{2}}$	7·22	2·3	38	6·00	3·0	21
J_4, $f(x) = (1-x)^{\frac{1}{3}}$	6·84	1·8	45	5·00	1·8	96
J_5, $f(x) = (1-x^2)^{\frac{1}{2}}$	6·68	1·7	77	5·26	1·6	50

* All constants were determined from linear plots.

be noted that the determination of v_m and m is independent of that of C. This is satisfactory because with both montmorillonite and attapulgite the C values are variable over a wide range. The intercepts from which C is derived are often small and the C values therefore uncertain. For larger values of C the form of the isotherm for bigger relative pressures does not depend very significantly upon C. In some instances (Table 3) C was

TABLE 3. *Nitrogen and ammonia on attapulgite.*

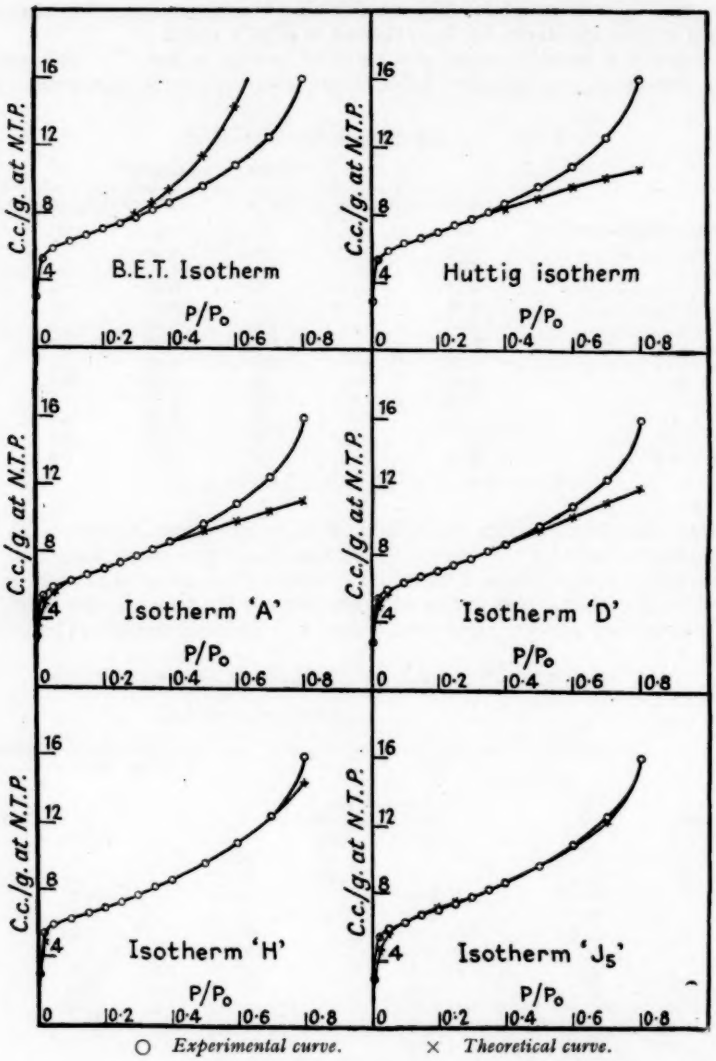
	Values of constants * for :							
	Nitrogen on sorbent outgassed at room temp.				Ammonia on sorbent outgassed at 625° K			
			C				C	
Isotherm designation	v_m	m	by substn.	from linear plot	v_m	m	by substn.	from linear plot
B.E.T.	43·81	—	—	∞	33·5	—	—	28·7
Huttig	47·19	—	—	170	33·22	—	—	43·0
A	46·66	—	200	—	32·64	—	41·5	—
B	40·62	—	2000	—	29·08	—	17·0	—
D	46·05	—	120	—	37·21	—	9·23	—
F	56·07	—	51	—	36·11	—	—	3·46
H	46·31	1·8	207	—	35·98	1·24	21·0	—
K_1, $f(x) = 1 - x$	47·34	3·0	145	—	39·47	2·2	15·5	—
K_2, $f(x) = 1 - x^2$	47·81	2·5	127	—	39·42	1·6	15·0	—
K_3, $f(x) = (1-x)^{\frac{1}{2}}$	46·78	2·1	175	—	40·42	1·8	13·1	—
K_4, $f(x) = (1-x)^{\frac{1}{3}}$	46·62	1·9	185	—	—	—	—	—

* v_m and m were in all cases determined from linear plots.

determined (after finding v_m and m from the linear plot) by employing a point on the experimental isotherm to fix this final constant. One is bound to conclude that the variability of C as between the isotherms should make one interpret it with caution; C is nevertheless more consistent when only the better-fitting isotherms are considered (see below).

The constant of greatest importance is v_m. For montmorillonite over the complete group of isotherms of Table 2 and with the mineral activated by outgassing at 523° K and 323° K the extreme ratios in the values of v_m for nitrogen at 78° K are 1 : 1·54 and 1 : 1·57 respectively. With the mineral outgassed at 323° K the best theoretical isotherms among

FIG. 3. *Sorption of nitrogen on montmorillonite outgassed at 523° K. Sorption temp. 78° K. See Table 2 for relevant values of* m.



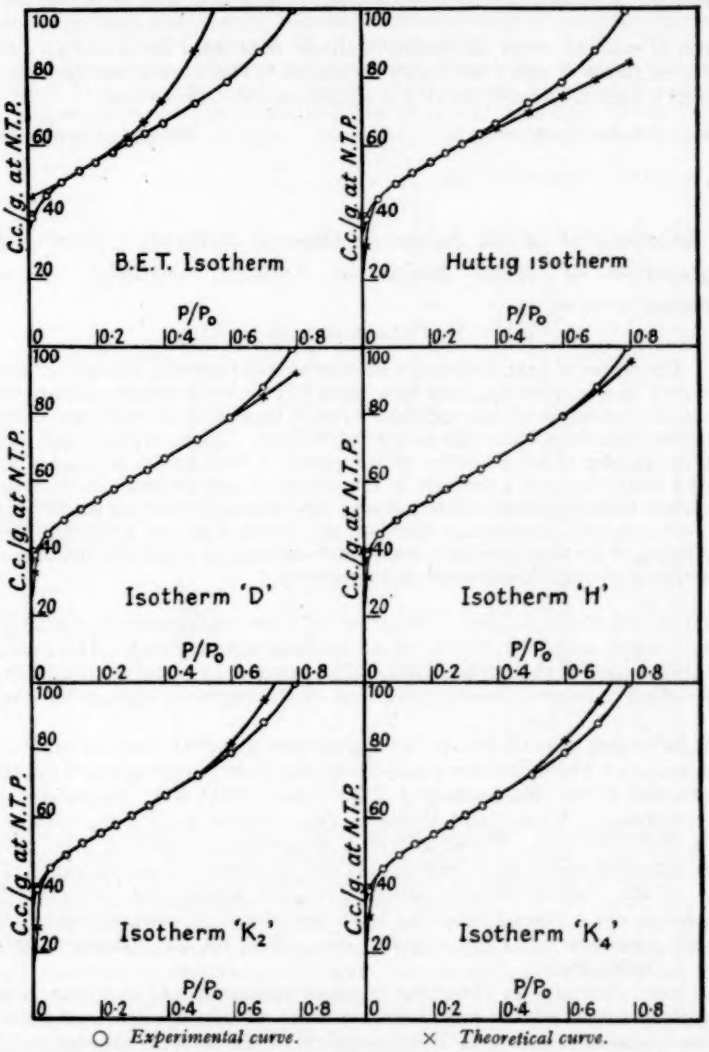
○ *Experimental curve.* × *Theoretical curve.*

those used are H, J_4, and J_5, for which the extreme ratio in v_m is 1 : 1·14. Including the, in this case, less satisfactory B.E.T. and Huttig isotherms the above ratio is 1 : 1·20. When the mineral was outgassed at 523° K the best theoretical isotherms are A, D, H, and J_5 (cf. Fig. 3), giving the extreme range in v_m of 1 : 1·15.

For sorption of nitrogen (at 78° K) on attapulgite outgassed at room temperature, and for ammonia (at 209·5° K) on this mineral outgassed at 625° K, the isotherms employed and

the relevant constants are shown in Table 3. The extreme ratios in v_m are 1 : 1·39 for ammonia, and 1 : 1·38 for nitrogen. The best isotherms for ammonia are *H*, K_1, K_2, and K_3, for which the ratio in v_m drops to 1 : 1·12. The best isotherms for nitrogen (cf. Fig. 4) are *D*, *H*, K_2, and K_4, for which the extreme ratio in v_m drops to 1 : 1·04. One may

FIG. 4. *Sorption of nitrogen on attapulgite outgassed at room temperature for* 14 *days. Sorption temp.* 78° K. *See Table* 3 *for relevant values of* m.



○ *Experimental curve.* × *Theoretical curve.*

therefore conclude that if, as would normally be the case, one considers only isotherms which are best able to represent the data, satisfactory agreement is found between values of v_m derived from these isotherms. The absolute value of the surface area so found may then be an accurate one.

On the other hand, many authors have used theoretical isotherms (*e.g.*, B.E.T. and Huttig equations) to derive surface areas from sorption data which these isotherms do

not fit well. In such cases the data in Tables 2 and 3 show that v_m values may differ substantially from corresponding values obtained by using better-fitting theoretical isotherms. The use of poorly-fitting theoretical isotherms could be a misuse of the adsorption method, leading to surface areas of low accuracy. However, a theoretical isotherm which fits poorly the experimental data for one sorbent may represent satisfactorily sorption data obtained with a second sorbent, perhaps because of different pore geometry. Examples of such behaviour were found among isotherms *A*, *B*, *D*, and *F*.

Isotherm *H* was uniformly successful in all our data (cf. Figs. 3 and 4). Also certain of the isotherm forms *K* and *J* were very successful. These are three-constant equations, so one cannot attach particular theoretical significance to their success.

MARISCHAL COLLEGE, ABERDEEN. [*Received, November 23rd*, 1951.]

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322. *Solutions of Metal Soaps in Organic Solvents. Part III.* The Aggregation of Metal Soaps in Toluene, iso*Butyl Alcohol, *and Pyridine.*

By S. M. NELSON and R. C. PINK.

The degree of aggregation of a number of metal soaps in toluene, *iso*butyl alcohol, and pyridine has been investigated by an ebullioscopic method. In toluene, the degree of aggregation is strongly dependent on the length of the hydrocarbon chain and on the polarity of the soap. The more polar soaps form larger micelles or are insoluble, while increase of chain length in soaps of the same metal leads to a decrease in the degree of aggregation. In the polar solvents *iso*butyl alcohol and pyridine the associating effect of the soap dipoles is reduced and unimolecular solutions are obtained at low concentrations. Stability of the soap micelles is due to diple interaction and to the decrease in interfacial energy which occurs on aggregation.

PART I (Martin and Pink, *J.*, 1948, 1750) recorded some measurements of micellar weights of zinc and copper soaps by means of an ebullioscopic method. The present report describes the extension of the method, by aid of an improved apparatus, to a variety of metal soaps. The effect of solvent dielectric constant on the degree of aggregation has also been examined.

Little information is available on the aggregation of metal soaps in organic solvents. Most of the soaps for which data are available appear to form aggregates of micellar weight between 2000 and 10,000 (Kahlenberg, *J. Phys. Chem.*, 1902, **6**, 1; Soyenkoff, *ibid.*, 1930, **34**, 2519; Bhatnagar, Kapur, and Hussain, *Proc. Indian Acad. Sci.*, 1939, **9**, *A*, 143; Martin and Pink, *loc. cit.*). These scattered observations, made in most cases over a limited concentration range, have been insufficient to permit an evaluation of the relative importance of the various factors involved in the aggregation process. The basic aluminium soaps are a special case and have not therefore been included in this study (cf. Gray and Alexander, *J. Phys. Colloid Chem.*, 1949, **53**, 23; Glazer, Schulman, and McRoberts, *J.*, 1950, 2082).

There is some difficulty in obtaining accurate measurements in this micellar weight range. Cryoscopic methods are unsuitable since the metal soaps frequently show critical solution phenomena well above the freezing points of the solvents (Martin and Pink, *loc. cit.*). Osmotic-pressure measurements with cellulose-type membranes are stated to be unsatisfactory for solutes with micellar weights below 10,000 (Weissberger, "Physical Methods of Organic Chemistry," Vol. I, p. 488, Interscience, 1949). Studies of sedimentation equilibrium and sedimentation velocity are also better suited to a higher micellar weight range (Alexander and Johnson, "Colloid Science," Vol. I, p. 188,

* Part II, *J.*, 1951, 1804.

Clarendon Press, 1949). On the other hand, conventional vapour-pressure methods and the ebullioscopic method, used in the present work, require special precautions if accurate measurements are to be obtained with micellar weights above 2000.

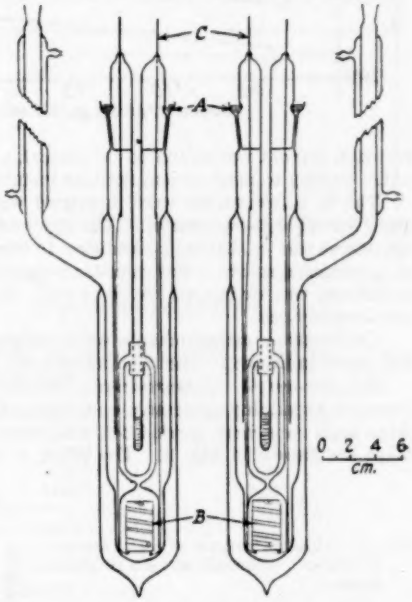
Experimental

Preparation and Purification of Materials.—Lauric, myristic, and oleic acids were pre-war " purissimus grade " samples from Schering–Kahlbaum. The remaining acids were purified, where necessary, by fractional crystallisation from ethanol; their m. p.s were: octanoic, 16·0°; decanoic, 31·1°; lauric, 44·1°; myristic, 57·5°; stearic, 69·2°; oleic, 15·0°.

All the metal soaps were prepared by metathesis of the corresponding sodium soaps in aqueous ethanol (Pink, *J.*, 1938, 1252). The precipitated soaps were washed with water and ethanol to remove excess of precipitant and free fatty acid and dried by various methods, depending on the properties of the soaps. The soaps prepared from saturated acids were dried

	Metal content, %: Found	Calc.
Zinc octanoate	19·11	18·58
Zinc decanoate	16·10	16·03
Zinc laurate	14·66	14·09
Zinc myristate	13·28	12·57
Zinc stearate	10·52	10·34
Zinc oleate	10·73	10·40
Magnesium laurate	5·85	5·75
Calcium laurate	8·83	8·78
Manganese laurate	12·07	12·11
Nickel laurate	13·28	12·82
Copper laurate	13·79	13·76
Cadmium laurate	20·80	21·24
Mercuric laurate	32·72	33·48
Silver laurate	34·72	35·13
Lead laurate	34·84	34·20

Fig. 1. *Micellar-weight apparatus.*



in an air-oven at temperatures ranging between 60° and 95°, the magnesium, nickel, and manganese soaps having been first dehydrated in boiling toluene. Zinc oleate, which is susceptible to oxidation, was dried at room temperature *in vacuo* over phosphoric oxide. For analysis, the soaps were hydrolysed with 7N-sulphuric acid, and the metal contents of the hydrolysates determined by standard procedures, after the free fatty acid had been removed by filtration. The calcium and cadmium soaps were analysed in the monohydrated form. The results of the analyses, shown above, indicate that the materials obtained were the neutral soaps with, in most cases, a slight excess of metal.

Solvents. Rigorous drying was found to be the most important aspect of purification for satisfactory operation of the ebullioscopic apparatus. Thiophen-free toluene was dried over sodium metal, from which it was distilled in an all-glass apparatus, b. p. 110·2—110·6°; *iso*butyl alcohol was dried over baryta and distilled from calcium metal, b. p. 107·7—108·1°; " AnalaR " pyridine was stored over potassium hydroxide and distilled from the freshly fused alkali through a fractionating column immediately before use, b. p. 115·2—115·6°.

Micellar-weight Apparatus.—The ebullioscopic apparatus was essentially a modified version of that employed by Mair (*J. Res. Nat. Bur. Stand.*, 1935, **14**, 345). A scale drawing of the apparatus, the dimensions of which are important, is shown in Fig. 1. Mercury sealing (*A*) was

used to prevent loss of solvent from the twin boiling tubes, and solute was added directly through the condenser openings. The heating units (*B*), which were 24·3 and 24·8 Ω severally, were of 36-gauge Brightray resistance wire jointed by 26-gauge nichrome leads to tungsten rods (*C*) sealed through the B.40 ground-glass joint. The mains voltage, controlled by a Variac transformer, was used for heating. With 47·0 ml. of toluene in each of the boiling-tubes satisfactory ebullition was obtained with a current of 1·55 amp. The actual value of the current

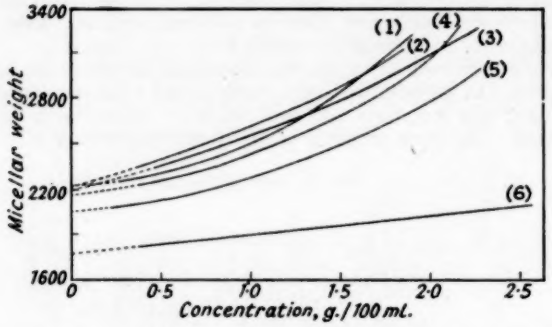


FIG. 2. *Micellar weights of zinc soaps in toluene. (Formula weights in parentheses.)*

(1) *Octanoate* (351·8).
(2) *Decanoate* (407·9).
(3) *Laurate* (464·0).
(4) *Myristate* (520·1).
(5) *Stearate* (632·3).
(6) *Oleate* (628·3).

for each solvent was found to be critical, a small variation in heater current from the selected value leading to marked temperature instability.

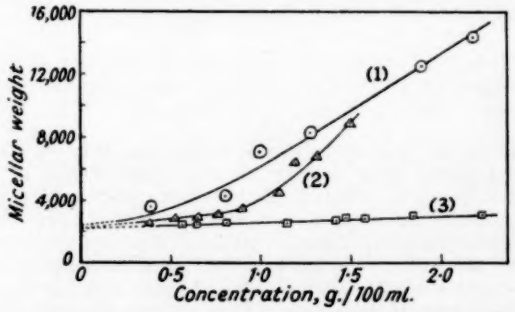
The b. p. elevations were measured with a five-junction copper–constantan thermocouple and a sensitive galvanometer. The absolute values were not calculated; instead, in each run the apparatus was calibrated by addition to the second vessel of a suitable quantity of naphthalene as a reference solute. For micellar weights of the order of 3000 the maximum error with this apparatus was estimated to be ±7%; for lower micellar weights the maximum error was considerably less.

Conductance measurements were made at 1100 c./second with a bridge employing a visual null-point indicator. The conductance cell had bright platinum electrodes.

Micellar-weight Measurements.—Micellar weights at a number of concentrations were obtained by adding successive quantities of solute to one of the twin boiling vessels. At least three such runs were carried out with every metal soap. The results obtained with the zinc soaps are shown in Fig. 2. The effect of different metals in soaps of the same chain length

FIG. 3. *Micellar weights of metal laurates in toluene. (Formula weights in parentheses.)*

(1) *Magnesium laurate* (422·9).
(2) *Copper laurate* (462·2).
(3) *Zinc laurate* (464·0).



is seen in Fig. 3 which contains data for a number of metal laurates. Calcium and cadmium laurates, although appreciably swollen in boiling toluene, were not completely dispersed. Lead and silver laurates were insufficiently soluble to permit measurements to be made, and nickel and manganese laurates, although soluble, gave galvanometer deflections which were too small for measurement, implying the presence of aggregates of micellar weight >20,000. Anomalous results were obtained with mercuric laurate, the observed molecular weight of which was lower than the formula weight. Analysis showed that decomposition took place in boiling toluene, the recovered soap containing 42·42% of mercury as against 32·75% in the original soap. According to Lawrence (*Trans. Faraday Soc.*, 1938, **34**, 660) the mercury soaps

decompose suddenly on heating, forming metallic mercury and a mixture of anhydride and acid. Mercuric laurate is stated by Lawrence to decompose at 210°.

Measurements in *iso*butyl alcohol and pyridine were made in exactly the same way as in toluene, the same reference solute being employed. Results obtained with zinc and copper laurates in these solvents are shown in Fig. 4.

Discussion

Solutions in Toluene.—Two broad conclusions emerge from the experimental data. First, the number of molecules (N) in the micelle decreases rapidly with increase in the length of the hydrocarbon chain. This is illustrated, for the saturated zinc soaps, in Fig. 5, where the value of N, extrapolated to infinite dilution, is plotted against the number of carbon atoms in the chain. The micellar weight similarly decreases but less rapidly. Secondly, in a series of soaps with the same hydrocarbon chains, the more polar soaps form larger micelles. Dipole moments for the oleates have been published by Banerjee and Palit (*J. Indian Chem. Soc.*, 1950, **27**, 385; cf. Ostwald and Riedel, *Kolloid-Z.*, 1934, **69**, 185) and their data are shown in the following table, together with micellar weights of the laurates of a number of metals at a uniform concentration of 0·02M.

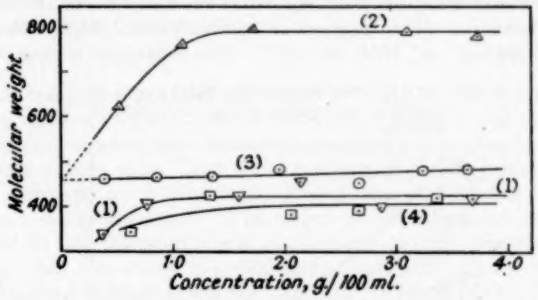


Fig. 4. *Molecular weight of zinc and copper laurates in polar solvents. (Formula weights in parentheses.)*

(1) *Copper laurate in pyridine.*
(2) *Copper laurate* (462·2) *in* isobutyl *alcohol.*
(3) *Zinc laurate* (464·0) *in* isobutyl *alcohol.*
(4) *Zinc laurate in pyridine.*

Metal.	Micellar weight of laurate	μ, D, for oleate
Zinc	2,600	0·29
Copper	3,500	1·20
Magnesium	6,000	1·66
Nickel	>20,000	2·67
Cadmium	Swells in toluene but does not dissolve at b. p.	4·37 *
Calcium	,, ,,	4·49
Lead	Insoluble	4·29

* Datum from Ostwald and Riedel (*loc. cit.*).

Increased polarity in this series corresponds closely with increase in micellar weight, some of the more polar soaps being insoluble at the b. p. of toluene. The zinc soaps differ also from the relatively more polar copper and magnesium soaps in the rapid increase in apparent micelle size of the latter which occurs with increasing concentration (Fig. 3). Although the non-ideal character of the solutions makes it difficult to distinguish sharply between Raoult deviations and real variations in micellar weight, yet the shape of the curves for the copper and magnesium soaps suggests strongly that the apparent increase in micelle size in this case is a real one. The increase in micellar weight with concentration shown by the zinc soaps is much less and could well be explained by departure from ideal behaviour. On the other hand, even with the zinc soaps, very concentrated solutions show a faint opalescence, indicating the presence of some very large micelles. It should be noted that all the quoted micellar weights are number averages and that a low average micellar weight in dilute solution does not, therefore, exclude the existence of some micelles of much larger size. A feature of the results in toluene, in contrast to those of the corresponding aqueous soap solutions, is the presence of aggregates at all observed concentrations. These conclusions, in conjunction, permit the development of a picture

of the aggregation process. In a non-polar solvent, aggregation is clearly the result of a balance between the solubilising power of the hydrocarbon chains and the attractive forces between the polar parts of the soap molecules. As is expected on this basis, the soaps with very short chains are insoluble, *e.g.*, the butyrates. On the other hand, with a sufficiently long chain the soap should be molecularly dispersed, unless other factors intervene. Unfortunately, acids with chains longer than 18 carbon atoms were not available to test this hypothesis.

An important factor favouring aggregation is the interaction between the soap dipoles which leads to a decrease in potential energy and a force of attraction, provided the soap molecules are suitably arranged in the micelle. Also favouring aggregation is the decrease in interfacial energy produced by the shielding effect of the hydrocarbon chains on the polar parts of the soap molecules which, in the micelle, are at least partially removed from contact with the non-polar solvent. In opposition to these factors is the kinetic energy of the soap molecules, which will be much reduced in the process of aggregation. Although the change in entropy on micelle formation must also contribute and may account largely for the effect of chain length on micelle size, yet it seems unlikely that it plays the same dominant rôle in aggregation as in aqueous soap solutions (Stainsby and Alexander, *Trans. Faraday Soc.*, 1950, **46**, 587). This is because in non-polar solvents, in contrast to aqueous

FIG. 5. *Effect of hydrocarbon chain length on degree of aggregation* (N) *of zinc soaps in toluene.*

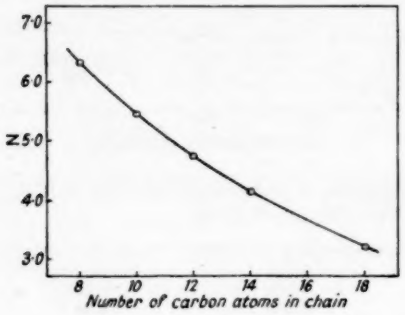
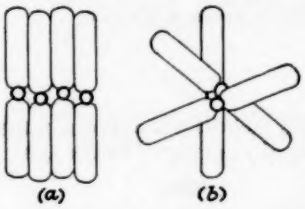


FIG. 6. *Packing of molecules in soap micelle in non-polar solvents.*



soap solutions, the environment of the hydrocarbon chains, before and after aggregation, is not greatly different. In the metal soaps studied in this investigation the balance of these various factors in non-polar solvents clearly favours aggregation. Also, different arrangements and different numbers of molecules in the micelle may lead to approximately the same decrease in free energy, when compared to the molecularly dispersed solute, so that various types of micelle may coexist in solution.

The strong dependence of micelle size on the polarity of the soap follows from Keesom's theory (*Physikal. Z.*, 1921, **22**, 126, 643; 1922, **23**, 225) according to which the average attractive potential $\bar{E}$ between two isolated dipoles is

$$\bar{E} = -2\mu_1^2\mu_2^2/3r^6kT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where μ_1 and μ_2 are the dipole moments of the two dipoles, r the distance between their centres, and k the Boltzmann constant. For a number of molecules, the total energy is the sum of all the pair interactions. In a metal soap solution in which the interacting species are identical, $\bar{E}$ is therefore proportional to μ^4; $\bar{E}$ can be calculated if we assign a value to r. Close approach of the dipoles in the aggregate is probably limited, in the first instance, by the hydrocarbon chains, and r, as an aproximation, may be taken as 5·2 Å, the cross-sectional diameter of the hydrocarbon chain, from monolayer measurements. This type of packing is illustrated in Fig. 6(*a*), which also indicates the structural arrangement found in the crystalline soaps as determined by *X*-ray measurements (Vold and Hattiangdi, *Ind. Eng. Chem.*, 1949, **41**, 2311). In the crystal, the chains are slightly

inclined to the plane containing the metal–carboxyl groups. For nickel laurate, therefore, with $\mu = 2{\cdot}67$ D (Table 3) and $T = 383°$ (b. p. of toluene), E has a value of $-1{\cdot}63 \times 10^{-14}$ erg per molecule. Since the total translational energy of the molecule at this temperature is $7{\cdot}88 \times 10^{-14}$ erg, it is clear that the decrease in potential energy due to dipole interaction alone is insufficient to stabilise the aggregate. This is true also of the less polar soaps of magnesium, copper, and zinc. On this basis, stabilisation of the aggregates must be due partly to the contribution from the interfacial-energy term, which is not so readily evaluated. The calculated value of the dipole interaction energy may, however, be too low for the following reasons. First, equation (1), which is derived on the basis of the simple Boltzmann statistics, is strictly applicable only to a phase in which free rotation is possible. For two dipoles, fixed relatively to one another, the interaction energy is given by

$$E = -\mu_1\mu_2[2\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2\cos(\phi_1 - \phi_2)]/r^3 \quad . \quad . \quad . \quad (2)$$

where θ and ϕ are polar co-ordinates giving the orientation of the dipoles whose moments are μ_1 and μ_2 at a distance r from each other, the polar axis being the line joining their centres. For the most favourable orientation this reduces to

$$E = -\mu_1\mu_2/r_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

With the same assumptions as before this gives for nickel laurate $E = -2{\cdot}53 \times 10^{-14}$ erg per molecule. In view of the marked asymmetry of the soap molecules, hindered rotation of the molecules in the micelle seems not improbable. Secondly, much higher interaction energies would be possible with lower values of r. Such close packing in the aggregate might occur if the molecules were arranged as in Fig. 6(*b*). Lastly, the significance of Banerjee and Palit's dipole-moment data is uncertain. The values of the moments are based on the assumption, common to all dipole-moment evaluations from dielectric-constant measurements on solutions, that the solute is molecularly dispersed. So far as zinc oleate is concerned this is definitely not the case in toluene (Fig. 2). It seems probable, therefore, that the calculated moments are too low, although there is no doubt that the measurements place the soaps in the correct *order* of polarity. The true value of the dipole interaction energy may thus be substantially greater than calculated from (1) above. Although it may be sufficiently large in the case of the more polar soaps to account alone for the aggregate stability, yet it seems likely that in all cases the decrease in interfacial energy also plays a significant part in the aggregation process.

Like the coulombic force between ions, the attractive force due to the dipoles is exerted indiscriminately on all other polar molecules depending only on the distance of separation. The tendency to form clusters through this effect is therefore of the same order of magnitude as that to form pairs provided that the distance of closest approach r does not vary with the size of the aggregate (cf. Hildebrand and Scott, "The Solubility of Non-Electrolytes," p. 56, 1950, Reinhold Publishing Corp.). From (1), E is obviously extremely sensitive to variation in this distance of closest approach of the dipoles. Once a metal soap micelle is formed, access of further molecules to the polar interior of the micelle may be hindered by the hydrocarbon chains, so that r may increase rapidly with increase in the size of the aggregate. This inability of the molecules to pack in the micelle in such a way that the maximum decrease in potential energy occurs probably represents a powerful limiting factor on the growth of the micelles in dilute solution. The steric factor is evident in the case of ferric laurate, which has three hydrocarbon chains. In solutions of this soap, aggregation stops at the dimer, partly because of the increased solubilising effect of three hydrocarbon chains as against two in the bivalent soaps, but also because of the steric hindrance to further aggregation provided by the six hydrocarbon chains of the dimer (Nelson and Pink, in the press). The low micellar weight of zinc oleate compared with that of the corresponding saturated soaps (Fig. 2) can probably be accounted for in the same way, the rigidity imparted to the chain by the centrally placed double bond in the oleate preventing close packing in the micelle. Zinc oleate and oleic acid itself have much lower m. p.s than the corresponding saturated compounds for analogous reasons. This difficulty in packing in the most favourable way in the micelle is accentuated by the fact that, at the

temperatures at which the soaps dissolve, the *hydrocarbon chains* are above their m. p. and the soaps themselves are often above well-marked mesomorphic transitions in the solid, akin to pre-melting phenomena (Vold, Grandine, and Vold, *J. Colloid Sci.*, 1948, **3**, 339; Hattiangdi, Vold, and Vold, *Ind. Eng. Chem.*, 1949, **41**, 2320; Martin and Pink, *loc. cit.*).

There is no reason to believe that the small micelles found in dilute solutions in toluene are other than roughly spherical in shape. Although some of the soaps separate from solution as a paste or pseudo-gel of very fine crystallites, dilute solutions exhibit none of the viscosity anomalies or gelling properties characteristic of systems containing strongly aniso-dimensional particles. Less can be said about the much larger micelles which appear to exist at higher concentrations in solutions of all the metal soaps; these may be analogous to the neutral lamellar micelles found in concentrated aqueous soap solutions, but much more evidence of a different kind is necessary to elucidate the problem of their structure.

Solutions in Polar Solvents.—Support is given to the theory outlined above by the results obtained in pyridine ($\varepsilon = 12{\cdot}5$) and *iso*butyl alcohol ($\varepsilon = 18{\cdot}7$). In these polar solvents a marked reduction in the aggregating effect of the soap dipoles is to be expected. As shown in Fig. 4, zinc laurate is molecularly dispersed over a wide range of concentration in *iso*butyl alcohol, as is copper laurate in dilute solution. In more concentrated solutions in *iso*butyl alcohol, however, the copper soap appears to aggregate to the dimer, a difference in accord with the more polar character of the copper soaps. In pyridine, the micellar-weight evidence suggests that both the zinc and the copper soaps are not only molecularly dispersed but partly dissociated into ions, the observed molecular weights being lower than the formula weights. Support for this view is provided by conductance data on pyridine solutions of copper laurate. A 0·063M-solution of this soap has a specific conductance of $2{\cdot}140 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$ as against $0{\cdot}1625 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$ for the pyridine itself. The increase in conductance, however, may be due partly to traces of fatty acid or copper sulphate in the soap.

The authors are indebted to Professor A. R. Ubbelohde, F.R.S., for helpful discussions.

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, December 19th*, 1951.]

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323. *The Delphinine Alkaloids. Part I.*

By G. R. CLEMO and BHOLA NATH.

From the seeds of *Delphinium staphisagria*, in addition to the known alkaloids delphinine and staphisine, a new crystalline base, $C_{29}H_{29}O_5N$, has been isolated and its ultra-violet absorption spectrum measured. On dehydrogenation with selenium, a phenanthrene-type hydrocarbon, $C_{18}H_{16}$, has been obtained.

The unsaponifiable non-basic fraction from the same seeds contains β-sitosterol.

SINCE the beginning of the nineteenth century many workers have examined the basic content of *Delphinium staphisagria* L. seeds (commonly known as stavesacre). In addition to delphinine ($C_{33}H_{45}O_9N$) and the recently isolated staphisine ($C_{22}H_{31}ON$ or $C_{42}H_{60}ON_2$), mention is made in the older literature (Marquis, *Arch. exp. Path. Pharmakol.*, 1877, **7**, 55—80; *Pharm. Z. Russland*, 1877, **16**, 449, 481, 513; Kara-stojanow, *Pharm. Z. Russland*, 1890, **29**, 628, 641, 657, 673, 689, 705, 721; abstracted in *Jahresber.*, 1877, 894—897, and *J.*, 1891, **60**, 842; Ahrens, *Ber.*, 1899, **32**, 1581) of the occurrence of other alkaloids, but none of these has been characterised.

Jacobs and Craig (*J. Biol. Chem.*, 1941, **141**, 67) recorded the presence of a very small quantity of a sparingly soluble alkaloid, m. p. 300° (decomp.), in the mother-liquors from delphinine and staphisine.

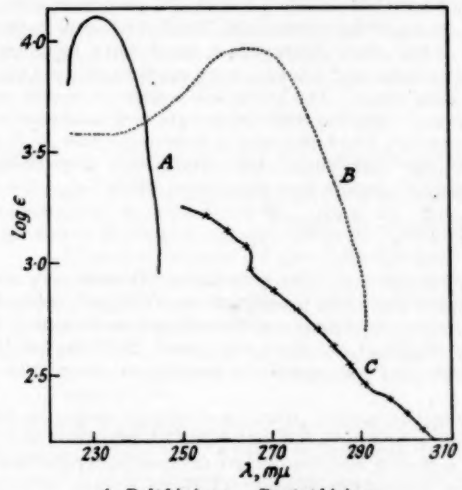
We have found that after delphinine and staphisine have been extracted from the

powdered seeds with light petroleum, chloroform removes further basic material from which a colourless crystalline base, $C_{20}H_{29}O_5N$, m. p. 286—290° (decomp.), can be obtained. This forms a crystalline oxalate, but only an amorphous hydrochloride and methiodide. On catalytic hydrogenation a dihydro-derivative is obtained.

The ultra-violet absorption spectra of delphinine, staphisine, and the new alkaloid have been compared. The values for the maxima of the first two alkaloids are in good agreement with those recorded (Jacobs and Craig, *loc. cit.*; Brustier and Vignes, *Bull. Soc. chim.* 1945, **12**, 37), but the nature of the curve for the new alkaloid is entirely different as shown in Fig. 1.

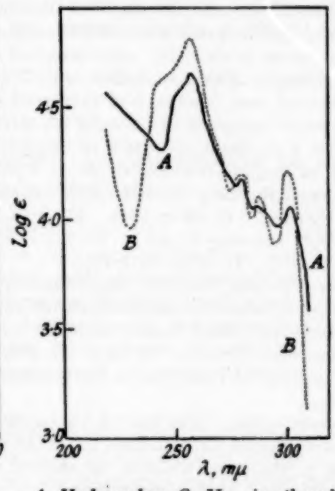
On dehydrogenation with selenium at 330—350° in nitrogen, the new base gives a mixture of hydrocarbons, of which only one has so far been isolated in a pure form. It melts at 51—52° and forms a picrate, and analyses indicate the formula $C_{18}H_{16}$. Its ultra-violet absorption spectrum (Fig. 2) clearly indicates that it is a phenanthrene derivative.

FIG. 1.



A, Delphinine; B, staphisine; C, new alkaloid.

FIG. 2.



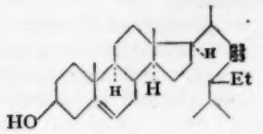
A, Hydrocarbon, $C_{18}H_{16}$, in ethanol; B, 1 : 2-cyclopentenophenanthrene.

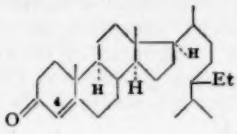
The nature of the curves, the positions and the intensities of the principal absorption maxima of various phenanthrene compounds lead to the conclusion that our hydrocarbon is either a *cyclo*penteno- or an alkyl-phenanthrene (Mayneord and Roe, *Proc. Roy. Soc.*, 1935, *A*, **152**, 317; Heilbronner, Daniker, and Plattner, *Helv. Chim. Acta*, 1949, **32**, 1723; Jacobs and Craig, *loc. cit.*; the *cyclo*penteno- and alkyl portions of these compounds do not produce any marked differences in the ultra-violet absorption, and it is not possible to decide on this evidence alone to which group our hydrocarbon belongs.

In 1927, Markwood (*J. Amer. Pharm. Assoc.*, 1927, **16**, 928), when reporting the insecticidal activity of the oil present in the seed of *D. staphisagria*, observed that the oil contains 2·92% of unsaponifiable matter. The latter has been investigated in this laboratory with the object of isolating pure compounds whose structure might have, directly or indirectly, some relation to the accompanying alkaloids. On chromatography the unsaponifiable portion yielded a number of substances, including β-sitosterol (22 : 23-dihydrostigmasterol) (I). The identity of this was confirmed by its conversion into β-sitost-4-enone (II), which was characterised as its oxime and dinitrophenylhydrazone.

By selenium dehydrogenation of staphisine Jacobs and Huebner obtained pimanthrene and retene, and in this laboratory the new alkaloid has also given a hydrocarbon containing

a phenanthrene nucleus. β-Sitosterol is the only accompanying phenanthrene derivative so far isolated in a pure condition from *D. staphisagria* seeds and may therefore be structurally related to the *Delphinium* alkaloids. Further work on the constitution of

(I) 



(II)

delphinine and other alkaloids of *D. staphisagria* seed and on the elucidation of the relation to the aconitine bases is in progress.

Experimental

Extraction of the Alkaloid.—The residue, after extraction of delphinine and staphisine by shaking the ground seeds with light petroleum (b. p. 40—60°) for 24 hours, was extracted (Soxhlet) with chloroform, and the dark oil thus obtained was extracted with 2% sulphuric acid. The combined acid extracts were washed with ether and light petroleum, basified (sodium hydroxide), and extracted with ether. On removal of the ether, light yellow, amorphous, basic material was obtained. This was shaken with 3% tartaric acid solution, then centrifuged, and the clear acid solution was basified and extracted with ether. The colourless residue from this extract was chromatographed in benzene on alumina. Elution with chloroform and methanol yielded a further very small quantity of delphinine and staphisine and a crystalline *base* (0·2—0·3 g. per kg. of commercial seeds), m. p. 270—280° (decomp.). Recrystallisation from methanol–ether raised the m. p. to 286—290° (decomp.) (slight colouration from 260°), $[\alpha]_D$ −19·23° in EtOH [Found: C, 66·4, 66·3; H, 8·15, 8·2; N, 3·9%; *M* (cryoscopic in bromoform), 368. $C_{20}H_{29}O_5N$ requires C, 66·1; H, 8·0; N, 3·9%; *M*, 363. Jacobs and Craig found for their base: C, 80·7; H, 8·8; N, 4·4%].

Salts.—To the base (12 mg.), dissolved in the minimum quantity of ethanol, were added a few drops of saturated alcoholic oxalic acid. The white precipitate was collected, washed with ether, and crystallised from ethanol, giving aggregated prisms of the *hydrogen oxalate*, m. p. 300—305° (decomp.) (Found: C, 58·5; H, 6·6. $C_{20}H_{29}O_5N,C_2H_2O_4$ requires C, 58·3; H, 6·8%).

An attempt to prepare a hydrochloride gave an amorphous precipitate, m. p. 290—295° (decomp.).

Hydrogenation.—The base (4·65 mg.) in methyl alcohol (10 ml.) containing a drop of acetic acid was hydrogenated with platinic oxide (15 mg.), hydrogen (0·3 ml.) being quickly absorbed. The reaction mixture was filtered, the solvent removed, and the *dihydro*-compound crystallised from methanol–ether, giving stout prisms, m. p. 235—238° (Found: C, 66·2; H, 8·8. $C_{20}H_{31}O_5N$ requires C, 65·75; H, 8·5%).

Dehydrogenation.—The alkaloid (1·1 g.) and selenium (4 g.) were heated in nitrogen to 345° for 6 hours. A trace of volatile material was trapped in an ice–salt mixture. The reaction mixture was extracted with hot benzene, the extract treated with 10% hydrochloric acid and then 5% sodium hydroxide solution, washed with water, and dried (Na_2SO_4), and the solvent removed. The oil was freed from selenium by distillation over sodium. The resinous product was chromatographed in benzene on alumina, and eluted with ether and chloroform. One fraction (20 mg.) distilled at 170—180° (bath-temp.)/0·2 mm., and when kept in a refrigerator for 2 days yielded a semicrystalline *hydrocarbon*. Crystallised from ethanol, this had m. p. 51—52° and showed a light blue fluorescence (Found: C, 93·5; H, 7·05. $C_{16}H_{16}$ requires C, 93·1; H, 6·9%). Its *picrate*, formed in ether and recrystallised from ethanol, had m. p. 145—147°.

Isolation of β-Sitosterol.—The alkaloid-free seed oil (225 g.) and methanolic potassium hydroxide (1 l.; 2N) were heated under reflux overnight. Part of the methanol was distilled off and the residue poured into water and extracted with ether. After removal of the ether, the residue was again heated with methanolic potassium hydroxide (125 ml.; 2N) for 2 hours and the mixture treated as before. The ethereal extract was washed twice with water, dried (Na_2SO_4), and distilled, yielding a semi-solid material (6·9 g., 3·1%). This was chromatographed in benzene–light petroleum (b. p. 40—60°) (1 : 1) on alumina and eluted with ether and chloroform. In the initial fraction a low melting solid (4·5 g.) with a terpene-like odour was obtained, but this was followed by the steroid (250 mg.) which gave colourless, shining plates (from methanol), m. p. 137—138°, $[\alpha]_D$ −31·90° (Found: C, 84·0; H, 12·4. Calc. for $C_{29}H_{50}O$: C, 84·1; H,

12·1%). It gave the Liebermann, Liebermann–Burchard, Salkowski, Rosenheim, and Tschugajeff colour tests.

The acetate, prepared in acetic anhydride–pyridine and crystallised from methanol, formed colourless prisms, m. p. 127°, not depressed by admixture with authentic material (Found: C, 81·2; H, 11·05. Calc. for $C_{29}H_{49}\cdot OAc$: C, 81·6; H, 11·4%).

The benzoate formed colourless prisms (from ether–methanol), m. p. 141°, not depressed by admixture with an authentic specimen (Found: C, 83·2; H, 10·9. Calc. for $C_{29}H_{49}O\cdot CO\cdot C_6H_5$: C, 83·4; H, 10·5%).

The digitonide (30·8 mg.) was obtained from the sterol (7·8 mg.).

The sterol (300 mg.) in acetone (6 ml.) was refluxed with aluminium *tert.*-butoxide (600 mg.) in benzene for 24 hours. The solution was washed with 2N-sulphuric acid and then water. After drying (Na_2SO_4) and removal of mesityl oxide, the product was chromatographed in light petroleum on alumina and eluted with benzene and ether. β-Sitost-4-enone (100 mg.) was obtained, having m. p. 87—88°, $[\alpha]_D$ +85·50° in ethanol (Found: C, 84·3; H, 11·6. Calc. for $C_{29}H_{48}O$: C, 84·5; H, 11·6%). Barton and Jones (*J.*, 1943, 599) have recorded m. p. 88° and $[\alpha]_D$ +85·88°.

The 2 : 4-dinitrophenylhydrazone was obtained as red prisms, m. p. 251—253° (decomp.) [Jones, Wilkinson, and Kerlogue, *J.*, 1942, **391**, report m. p. 253° (decomp.)], and the oxime as colourless prisms, m. p. 177° (*idem, ibid.*, record m. p. 175—175·5°) (Found: C, 80·95; H, 11·3. Calc. for $C_{29}H_{49}ON$: C, 81·5; H, 11·5%).

KING'S COLLEGE, NEWCASTLE-ON-TYNE, 1. [*Received, December 27th*, 1951.]

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324. *A Study of the Variations produced by Sublimation in the Infra-red Spectra of Some Substituted Succinic Acids.*

By L. A. DUNCANSON.

Changes observed in the infra-red spectra of (±)-methylsuccinic acid, (+)-methylsuccinic acid and (±)-chlorosuccinic acid after sublimation are reported. These changes are best explained by assuming that the sublimates contain at least one other rotational isomer than is present in the original crystallised form. Confirmatory evidence for the existence of rotational isomers of (±)-methylsuccinic acid has been obtained from dipole-moment measurements.

WHILE establishing the identity of a sample of methylsuccinic acid by means of its infra-red spectrum, it was noticed that purification of the acid by sublimation produced specimens with low melting points and marked changes in their infra-red spectra when compared with those of samples purified by recrystallisation from solution (Grove, MacMillan, Mulholland, and Zealley, to be published). That the changes were not due to anhydride formation was ascertained by means of chemical analysis and by the fact that no characteristic anhydride bands were found in the spectra near 1800 cm.$^{-1}$. In addition, it has been reported by Adams and Anderson (*J. Amer. Chem. Soc.*, 1951, **73**, 136) that molecular distillation of dibasic and methyl-substituted dibasic acids at temperatures much higher than those used in the present work does not cause anhydride formation. These observations seemed to require investigation from the point of view of the characterisation of organic molecules by their infra-red spectra, if for no other reason, and the results of a qualitative study of the cause of such changes are now reported.

Similar changes were observed in the infra-red spectra of (±)- and racemic methylsuccinic acids and of (±)-chlorosuccinic acid after sublimation. Sublimation of *as*-dimethylsuccinic and *meso*-dichlorosuccinic acids caused their melting points to be lowered but no change was produced in their spectra, but malonic and glutaric acids showed no change in either melting point or spectra on sublimation.

EXPERIMENTAL

Spectroscopic Measurements.—The infra-red spectra were all obtained from solid samples of the acids which were ground to fine powders and suspended in thin films of "Nujol" between two rock-salt plates. The spectra of crystallised and sublimed samples of (±)-methylsuccinic

acid in the regions of " Nujol " absorption (7μ and 3μ) were obtained by suspending the powdered acids in hexachlorobutadiene.

A modified Hilger D.209 spectrometer was used, working as a single-beam instrument and fitted with a 30° rock-salt prism on a Littrow mounting. Absorption due to atmospheric water vapour was reduced to a low level by enclosing the instrument in an air-tight " Perspex " case through which dry air was circulated. Hydrocarbon bands of known frequency, together with atmospheric carbon dioxide and residual water vapour bands, were used for frequency calibration. The calibration is considered to be accurate to ± 3 cm.$^{-1}$ in the region 750—1800 cm.$^{-1}$ and to ± 10 cm.$^{-1}$ at higher frequencies. During the recording of spectra from 750 cm.$^{-1}$ to 1800 cm.$^{-1}$ the spectrometer slit was closed in stages from a width of 0·6 mm. at the longer wave-length end of this range to 0·06 mm. at the shorter. The energy background was measured by replacing the samples by two rock-salt plates of the same thickness as those used for supporting the samples, and the absorption curves were then plotted in the usual way. No allowance was made for scattered radiation and therefore, although approximately equivalent sample thicknesses were used for each spectrum, it is not possible to compare the intensities of the bands in any one spectrum with those in another. However, as the slit widths were constant for approximately the same frequency ranges in each spectrum, it is possible to compare the relative intensities of the bands in any one spectrum with the relative intensities of those in others.

Preparation of Samples.—Commercial samples of malonic, succinic, glutaric, (±)-chlorosuccinic, and *meso*-dichlorosuccinic acids were recrystallised to constant m. p. from suitable solvents. (±)-Methylsuccinic acid was prepared as described in *Org. Synth.*, **26**, p. 54, and resolved through its strychnine salt (Ladenburg, *Ber.*, 1895, **28**, 1170). It had $[\alpha]_D^{19}$ +10°. *as*-Dimethylsuccinic acid was prepared by condensing acetone with cyanoacetic ester and addition of hydrogen cyanide to the resulting ethyl α-cyano-β-methylcrotonate, followed by hydrolysis and decarboxylation of the product in acid solution.

Microanalyses for carbon and hydrogen, carried out by Mr. W. Brown on samples of methylsuccinic acid before and after sublimation, were found to be virtually identical (Found, for specimen crystallised from water and dried *in vacuo* at 20° over P_2O_5: C, 45·5; H, 6·1. Found, for a specimen sublimed at 80—90°/10^{-3} mm. and dried as above: C, 45·3; H, 6·0. Calc. for $C_5H_8O_4$: C, 45·4; H, 6·1%).

The acids were sublimed as follows, small molecular stills being used consisting of two concentric glass tubes held vertically and closed at their lower ends. The tubes fitted together at their upper ends by means of a standard joint, the free space separating their lower ends being about 5 mm. A small amount of the acid to be sublimed was placed in the bottom of the outer tube, cold water was circulated through the inner tube and the annular space between the tubes evacuated by means of a mercury-diffusion pump. The lower end of the still was then placed in an oil-bath which was heated to, and kept at, the required temperature. The temperature of the oil-bath and the pressure inside the still in each case are given in Table 1, together with observed m. p.s of the acids. The melting points are uncorrected but the same thermometer was used for the comparison of melting points before and after sublimation.

TABLE 1.

Acid	Solvent for recrystn.	M. p.	Conditions of sublimation (°c/mm. Hg)	M. p. after sublimation
Malonic	Benzene–ether	134°	70—80/3 × 10^{-4}	134°
Succinic	Water	186	70—80/3 × 10^{-4}	181—182
Glutaric	Benzene–ether	96—98	55—60/5 × 10^{-4}	96—98
(±)-Methylsuccinic ...	Chloroform–light petroleum	113—114	150/5 × 10^{-4}	110—111
	Water	113—114	70—80/5 × 10^{-4}	108—109
(+)-Methylsuccinic ...	Benzene	106—107	90/3 × 10^{-3}	105—106
as-Dimethylsuccinic ...	Water	141—142	70—75/5 × 10^{-4}	137—139
	Water	141—142	155/5 × 10^{-4}	141—142
(±)-Chlorosuccinic ...	Ethyl acetate–light petroleum	152—153	65—70/3 × 10^{-4}	146—148
meso-Dichlorosuccinic	Ether–light petroleum	217 (d)	145/3 × 10^{-3}	204—206

Dipole-moment Measurements.—The dipole moments of the sublimed and crystallised forms of (±)-methylsuccinic acid in benzene solution were measured by Dr. R. G. Wilkins. All the measurements were made at 25° in an apparatus based on that of Hill and Sutton (*J.*, 1949, 2313). The use of very dilute solutions was necessitated by the low solubility of both forms of the acid in benzene, but this had the advantage of reducing intermolecular association. Complications arising from this last effect were minimised by using approximately the same concentration of

the solutes for all the measurements. Even at the low concentrations used (0·006M) the solutions appear to be supersaturated, for gentle warming was necessary in their preparation, and after standing for a day in a stoppered flask at room temperature the solutes invariably crystallised out.

The moments were calculated in the usual way by using Jensen's approximate formula (*Acta Chem. Scand.*, 1949, **3**, 479) for the total polarisation (P_M) and the usual relationship $P_O = P_M - P_R$, for the orientation polarisation, where P_R is the refractivity of the solute calculated from the bond refractivities. Finally, the dipole moment was obtained in Debye units: $\mu = 0{\cdot}22\sqrt{P_O} = 0{\cdot}22\sqrt{P_M - P_R}$. Two measurements were made on each form of (±)-methylsuccinic acid, and the results are given below:

(i) (±)-Methylsuccinic acid (crystallised form)

10^3C	ε_s	P_M	P_R	P_O	μ, D
6·092	2·2735	26·3	28·35	0	0
6·169	2·2738	34·0	28·35	5·65	0·52

(ii) (±)-Methylsuccinic acid (sublimed form)

10^3C	ε_s	P_M	P_R	P_O	μ, D
6·212	2·2742	45·1	28·35	16·75	0·90
6·289	2·2745	52·5	28·35	24·15	1·08

Results

The frequencies of the absorption bands in the spectra of (±)- and (+)-methylsuccinic acid, together with those of (±)-chlorosuccinic acid, throughout the region 750—1750 cm.$^{-1}$ are listed in Table 2, and some of the absorption spectra are presented in Figs. 1 and 2. In the following paragraphs some of the salient features of the various spectra are noted.

(±)-*Methylsuccinic acid.* In Fig. 1 are shown the spectra of (±)-methylsuccinic acid when (*a*) crystallised from water, (*b*) sublimed at 70—80°/5 × 10^{-4} mm., (*c*) sublimed at

Table 2. *Frequencies (in cm.$^{-1}$) of absorption bands of some substituted succinic acids before and after sublimation.*

(Figures in parentheses denote shoulders on the sides of other bands. The letters denote band intensities as follows: vw = very weak, w = weak, m = medium, s = strong, vs = very strong.)

(±)-Methylsuccinic acid		(+)-Methylsuccinic acid		(±)-Chlorosuccinic acid	
Crystallised	Sublimed	Crystallised	Sublimed	Crystallised	Sublimed
—	—	—	785 vw	—	780 m
—	—	—	812 vw	809 m	(810)
—	833 w	—	835 m	—	—
852 w	—	855 w	—	—	—
—	(880)	—	—	(870)	(890)
903 m	(900)	903 w	—	—	—
951 s	942 s	938 s	952 s	932 s	945 s
—	(970)	—	—	—	(965)
1048 vw	(1060)	(1055)	(1044)	—	—
1073 m	1081 m	1070 m	1087 m	—	1085 w
—	—	1098 vw	1108 w	—	—
1136 m	(1135)	1137 m	1140 w	—	—
—	1149 w	—	—	—	—
—	—	—	—	—	1192 m
1205 s	1210 s	1205 s	1210 s	1201 s	1208 s
—	1232 s	—	1233 s	1238 vw	—
1254 vw	—	(1255)	—	—	(1255)
—	1267 m	—	1261 s	—	—
(1300)	1297 m	—	1301 s	1307 s	(1295)
1331 s	—	1322 s	—	—	1315 s
—	1342 m	—	1347 m	—	—
1380 vw	(1380)	—	—	—	—
—	(1418)	—	(1417)	—	—
1435 s	1441 s	1430 s	1443 s	1437 s	1438 s
1475 m	(1470)	—	—	—	—
1701 vs	1701 vs	1705 vs	1705 vs	1723 vs	1723 vs

150°/5 × 10^{-4} mm. It can be seen that sublimation causes an increase in the number of absorption bands in the spectrum, the changes produced being summarised as follows. The band at 850 cm.$^{-1}$ is replaced by one at 830 cm.$^{-1}$. There is marked weakening of the band at 903 cm.$^{-1}$ and slight lowering in frequency of the 950 cm.$^{-1}$ band, a slight shoulder appearing on the side of the latter at about 970 cm.$^{-1}$. Two new weak bands appear at 1050 and 1150 cm.$^{-1}$ and a strong band appears at 1230 cm.$^{-1}$. The strong band at 1330 cm.$^{-1}$ with a shoulder at about 1300 cm.$^{-1}$ is replaced by three bands of lower intensity at 1264, 1296, and 1340 cm.$^{-1}$, and the band at 1435 cm.$^{-1}$ moves to a slightly higher frequency (1441 cm.$^{-1}$) revealing a slight shoulder

at about 1420 cm.$^{-1}$. However, no change can be detected in the frequency of the very strong band at 1700 cm.$^{-1}$, within the limits of experimental accuracy. At higher frequencies (2000—3500 cm.$^{-1}$), it is not easy to analyse differences between the spectra of crystallised and sublimed samples owing to the poor resolving power of the rock-salt prism in this region, but it appears that sublimation causes the absorption beginning at about 2400 cm.$^{-1}$ to get broader and less intense compared with the absorption maximum at 2900 cm.$^{-1}$.

Comparison of the three curves in Fig. 1 reveals that sublimation of the acid at 150° causes less strongly marked changes in its spectrum than does sublimation at 80—90°. This is shown,

FIG. 1. FIG. 2.

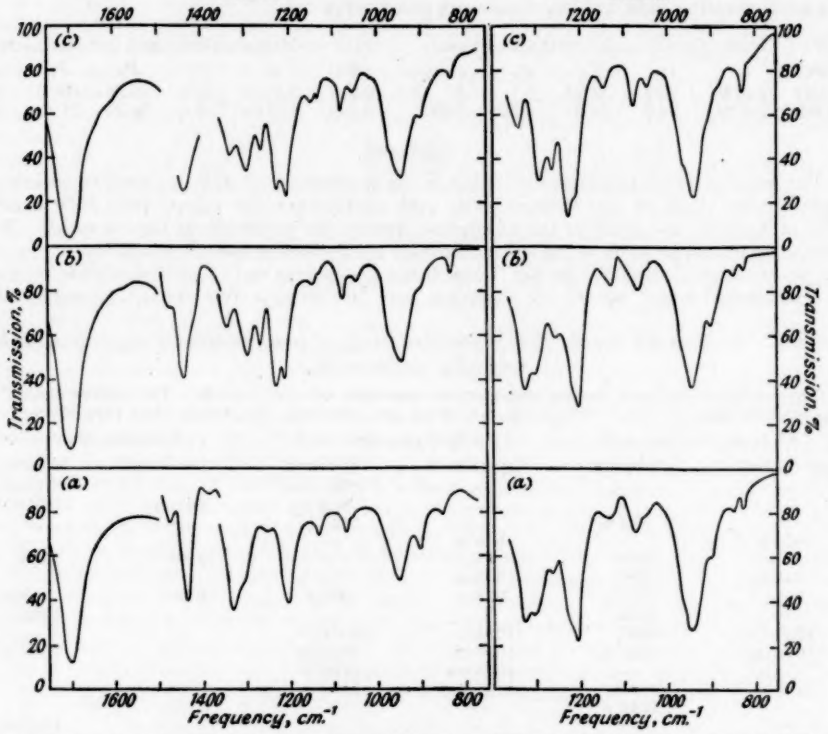


FIG. 1. *Infra-red spectra of* (±)*-methylsuccinic acid:* (a) *crystallised from water;* (b) *sublimed at* 70—80°/ 5 × 10^{-4} *mm.;* (c) *sublimed at* 150°/5 × 10^{-4} *mm.*

FIG. 2. *Infra-red spectra of sublimed* (±)*-methylsuccinic acid obtained after:* (a) *recrystallisation from aqueous solution at room temperature;* (b) *recovery from the sodium salt at room temperature;* (c) *refluxing its aqueous solution for* 30 *minutes.*

for example, by the strengths of the bands at 900, 1135, and 1230 cm.$^{-1}$ relative to those at 950—940, 1150, and 1205 cm.$^{-1}$, respectively.

Some experiments were performed to investigate the reconversion of the sublimed form of (±)-methylsuccinic acid into the crystallised form, and absorption curves between 750 and 1350 cm.$^{-1}$, obtained from the samples of the sublimed acid after various treatments in solution, are given in Fig. 2. Fig. 2*c* is the spectrum of the sublimed acid after it had been heated under reflux in aqueous solution for 30 minutes, and the solvent then completely removed at room temperature and reduced pressure over phosphoric oxide. The spectrum is little changed from that of the sublimed acid, the only significant difference being the relative intensities of the bands at 1230 and 1210 cm.$^{-1}$. Some of the solution used in this experiment was refluxed for a further 2 hours and the solvent then completely removed by standing in a desiccator over phosphoric oxide. The resulting acid had a spectrum (not shown) identical with that of the normal crystallised acid. A more dilute solution of the sublimed acid was then evaporated at room temper-

ature over phosphoric oxide and the recovered acid was found to have a spectrum in between those of the sublimed and the crystallised form (Fig. 2*a*). The reconversion seems therefore to be facilitated by using dilute solutions and this probably has two causes: (i) that the time taken to remove the solvent is increased, and (ii) that in aqueous solutions reconversion into the crystallised form proceeds more rapidly through the anion than through the acid itself. Both the 830 and the 850 cm.$^{-1}$ band were present, the 900 cm.$^{-1}$ band had begun to reappear, the 1230 cm.$^{-1}$ band was only apparent as a shoulder on the side of the 1205 cm.$^{-1}$ band, and the bands near 1300 cm.$^{-1}$ were nearly restored to those of the crystallised form. A similar result was found when some of the sublimed acid was converted into its sodium salt and then recovered, all the necessary operations being carried out at room temperature (Fig. 2*b*). Lastly, it was found that the sublimed acid could be recovered with an unchanged spectrum when recrystallised from non-polar solvents such as benzene and toluene.

(+)-*Methylsuccinic acid.* The spectrum of this acid, crystallised from benzene, is very similar to that of the (±)-modification crystallised from water, the main difference being that the band occurring at 950 cm.$^{-1}$ in the latter occurs at a slightly lower frequency in the former. The changes produced in the spectrum of the active form by sublimation are closely parallel to those found for the racemic form. The principal differences between the two cases are that with the active form the 950 cm.$^{-1}$ band is raised in frequency by sublimation, and although it is broad it shows no shoulders, that weak new bands occur at 785, 821, and 1108 cm.$^{-1}$, and that the relative intensities of the bands between 1200 and 1350 cm.$^{-1}$ are altered. Small differences in frequency of some of the bands also occur.

(±)-*Chlorosuccinic acid.* The spectrum of the crystallised acid is similar in form to that of crystallised methylsuccinic acid, as are some of the changes caused by sublimation; *e.g.*, strong bands occur at 932, 1201, 1307, 1437, and 1724 cm.$^{-1}$, together with a band of medium intensity at 810 cm.$^{-1}$. Sublimation causes the 810 cm.$^{-1}$ band to shift to a lower frequency, the 932 cm.$^{-1}$ band to shift to a higher frequency and to develop shoulders, a new band to appear near 1080 cm.$^{-1}$, the 1201 cm.$^{-1}$ band to split into two components, and lastly, the 1307 cm.$^{-1}$ band to become just resolvable into two components at 1290 and 1315 cm.$^{-1}$. As with (±)-methylsuccinic acid, the changes are less marked when the sublimation temperature is raised.

Other dibasic acids. Of the spectra of other dibasic acids which were measured during the present work, only the salient features will be mentioned here. They all show broad absorption bands in the region of 2600 cm.$^{-1}$ and very strong bands near 1700 cm.$^{-1}$. The acids with α-chloro-substituents have this band at slightly higher frequency than the others. Strong bands occur in all the spectra at 920—950, 1200—1230, 1300—1320, and near 1430 cm.$^{-1}$. Malonic and succinic acids both show two bands in the neighbourhood of 1700 cm.$^{-1}$, presumably owing to symmetrical and antisymmetrical modes of vibration involving C=O stretching. Substitution of comparatively heavy groups, such as methyl or chlorine, at the α-carbon atom seems to weaken the coupling between these two vibrations, for only one C=O band was observed in each of the spectra of dimethylmalonic, methylsuccinic, and chlorosuccinic acid.

Discussion

The bands near 2600 and 1700 cm.$^{-1}$ in the spectra of substituted succinic acids can be assigned quite definitely to vibrational modes involving the stretching of carboxylic O–H and C=O bonds respectively, the low frequency and broadness of the O–H stretching band compared with the O–H band of alcohols being indicative of strong hydrogen bonding between two carboxyl groups, as is well known (Davies and Sutherland, *J. Chem. Phys.*, 1938, **6**, 755).

Assignments of other strong bands characteristic of carboxylic acids to vibrations involving the carboxyl group are less certain. Davies and Sutherland (*loc. cit.*) have assumed from a variety of evidence that the vibration of acetic acid which involves the stretching of the C–O bond causes the absorption band in its spectrum near 1430 cm.$^{-1}$, an assignment in agreement with that of Gillette and Daniels (*J. Amer. Chem. Soc.*, 1936, **58**, 1139). It has also been suggested by Davies and Sutherland that the bands near 1250 and 930 cm.$^{-1}$ are probably due to in-plane and out-of-plane deformation modes of the hydroxyl group. However, Flett (*J.*, 1951, 962) found that many carboxylic acids do not show a strong band in their spectra near 1400 cm.$^{-1}$ and concluded that it is not a good diagnostic band for this type of compound.

The case of the unsymmetrically substituted succinic acids is somewhat different in

that two vibrations involving the stretching of C–O bonds should be observed, and the author considers it at least as likely that these modes are responsible for the bands near 1200 cm.$^{-1}$ as that one of them is the cause of the band near 1430 cm.$^{-1}$. Support for this assignment is given later.

Having considered some of the probable causes of absorption in the spectra of the dibasic acids it now becomes of interest to discuss the changes produced by sublimation. This requires some enquiry into the process of sublimation which, for convenience, we can divide into three stages, namely, evaporation, passage through a vapour phase, and condensation. It is well known from spectroscopic and other data that carboxylic acids in the solid state are associated through their carboxyl groups, and that at low pressures and high temperatures the vapour consists to a large extent of the monomeric form. It can therefore be assumed that the first stage of sublimation in a high vacuum causes considerable dissociation of an acid from the dimeric (or possibly with dibasic acids, polymeric) form to the monomeric form. The values of the hydroxyl and carbonyl stretching frequencies of the sublimed acids show that the reverse occurs on condensation, *viz.*, association by hydrogen-bond formation between the carboxyl groups.

Changes in the vibrational spectra of the acids after sublimation might be expected on the grounds that the molecular environment had changed owing to the rapidity of condensation having prevented the formation of the most stable crystalline form, the intermolecular forces thereby being altered. However, this alone does not explain the following points. First, not all the acids investigated showed changes in their spectra after sublimation under identical conditions; secondly, it was found possible to recrystallise the sublimed form of (±)-methylsuccinic acid without causing any significant change in its spectrum, and lastly, the changes produced by sublimation are considered to be too great to be solely attributable to such a cause. However, imperfect crystal formation may well account for the lowering of the m. p.s of the acids after sublimation.

The spectra of crystallised and sublimed forms might also be expected to be different for the same reason as was put forward by Lecomte to explain the differences between the infra-red spectra of the salts of optically active and racemic tartaric acids (" Contribution à l'Étude de la Structure Moleculaire," p. 137, Maison Desoer, Liége, 1947—48). He suggested that crystals of the racemate consist of D- and L-molecules arranged in pairs in such a way that every pair has a centre of symmetry, thereby rendering some of the molecular vibrations inactive towards infra-red absorption. Such an arrangement, necessitating the presence of both optical antipodes in the crystal, cannot take place with either one or other of the active forms, and this explanation was put forward for the occurrence of considerably fewer bands in the spectra of the racemic salts than in those of the optically active ones. It was found in the present work that, although the only two acids which showed changes in their spectra after sublimation contained asymmetric carbon atoms and sublimation might be expected to destroy to some extent the " pairing " of (+)- and (−)- molecules, yet this explanation does not accommodate the fact that the dextrorotatory form of methylsuccinic acid shows parallel changes on sublimation to those found with the (±)-acid. Furthermore, if molecules of this type tended to attain the most symmetrical arrangement by " pairing " in the solid state, *as*-dimethylsuccinic acid would be expected to do so. In fact, no changes were produced in the spectrum of the latter compound by sublimation, and it is concluded that this, in conjunction with the behaviour of (+)-methylsuccinic acid, rules out any explanation of the above type for the phenomena described in this paper. However, the differences between the spectra of (±)- and (+)-methylsuccinic acids may be due to this cause.

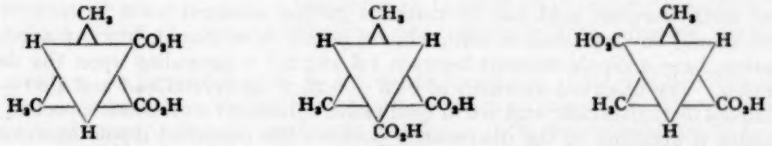
It is in the vapour stage of the sublimation process that a state of affairs can be postulated which accounts qualitatively for all the effects produced by sublimation. It has already been assumed that the vapour stage consists, to some unspecified extent, of single molecules of the acid being sublimed and these molecules are presumably able to undergo internal rotation about one or more of their single bonds. If it is assumed that, under the conditions used, the rate of rotational isomerisation is sufficiently high compared with the average rate of passage through the vapour to the condensed phase, then the sublimate should consist of more than one rotational isomer. A considerable amount of

evidence has been accumulated which demonstrates the occurrence of rotational isomerism in liquid disubstituted ethanes, such as 1 : 2-dihalogenoethanes, and in *n*-propyl bromide (see Mizushima *et al.*, *J. Chem. Phys.*, 1949, **17**, 591; Brown and Sheppard, *Discuss. Faraday Soc.*, 1950, No. 9, 148; Beach, *Ann. Rev. Phys. Chem.*, 1950, **1**, 196), but so far it has not been possible to obtain more than one rotational isomer of this type in the solid state. However, rotational isomerism in the solid state is well known in the case of heavily *o*-substituted diphenyls and has been reported for tin and lead tetraethyls (Staveley *et al.*, *J.*, 1950, 2290). With succinic acids the position is complicated by the fact that rotation can occur about the bonds connecting the carboxyl carbon atoms to the hydrocarbon nucleus in addition to rotation about the central carbon–carbon bond.

The changes produced in the spectra by sublimation are consistent with the occurrence of rotational isomers. In the first place, the changes are so marked that they must be due to some considerable change in the molecular configuration. Also, it can be seen that one of the most characteristic changes is the splitting of the band which occurs near 1200 cm.$^{-1}$ in all the spectra into two components. It has already been suggested that bands near 1200 cm.$^{-1}$ can be attributed to modes involving the stretching of carboxylic C–O bonds, and that in monosubstituted succinic acids there should be two such modes. If the crystallised forms of the acids have the carboxyl groups situated *trans* to each other (as is probable), one of these modes will produce only a weak infra-red absorption which could well be masked by the strong absorption due to the other. The rotational isomers which are possible would have the carboxyl groups less symmetrically situated and then both C–O stretching modes would cause strong absorption and two bands should be observed.

The behaviour of the disubstituted and unsubstituted succinic acids can be understood if the interpretation of the behaviour of the monosubstituted acids as due to rotational isomerisation is correct. The case of the disubstituted acids being taken first, there are three possible reasons why they show no changes in their spectra after sublimation, *viz.*, (i) that the hindrance to internal rotation is large enough to prevent any appreciable isomerisation during the passage of molecules through the vapour phase; (ii) that the energy difference between the isomers is so great that even at the temperature of sublimation the equilibrium strongly favours the most stable isomer; (iii) that the energy difference between permissible isomers is so small that the equilibrium between them is fairly independent of temperature. Neglecting rotation of the methyl and carboxyl groups and assuming that staggered configurations are the most stable (Beach, *loc. cit.*), we can see that there are three possible rotational isomers of, say, *as*-dimethylsuccinic acid. Of these, two [Fig. 3, (*a*) and (*b*)] are equivalent and an equilibrium involving them alone would not be temperature-variable. In addition, these two isomers, being mirror images, would be indistinguishable by their infra-red spectra. If such an equilibrium is present during sublimation, then the formation of the third isomer [Fig. 3 (*c*)] must be prevented either by a high activation energy for rotation of a carboxyl group past a β-methyl group or else by the third isomer being very unstable. Alternatively, the third isomer is the most stable one and the transition to either of the other two is not achieved under the conditions of sublimation. Similar considerations apply to the case of *meso*-dichlorosuccinic acid.

FIG. 3.



Two factors provide explanations for the difference in behaviour between succinic acid and its monosubstituted derivatives. First, the rate of isomerisation must be greater in the former than in the latter case as there is one less bulky substituent to hinder internal rotation; *i.e.*, the potential energies of the "eclipsed" configurations of succinic acid are less than those of the corresponding configurations of the monosubstituted acids. The

activation energy for isomerisation thus being lower for succinic acid than for, say, methylsuccinic acid makes it more difficult to " freeze " the equilibrium present in the vapour by condensation on a cold surface. The second factor is that the difference in energy between the two most probable rotational isomers of methylsuccinic acid (Fig. 4) is expected to be less than that between the isomers of succinic acid. An analogous pair of molecules for which the equilibrium between rotational isomers has been compared consists of propylene dichloride and ethylene dichloride. Morino, Miyagowa, and Haga (*J. Chem. Phys.*, 1951, **19**, 791) have pointed out that the former has a smaller energy difference between two of its isomers than has ethylene dichloride because of the repulsion between the methyl group and a chlorine atom, which occurs in its low-temperature form, but not in its next most stable isomer.

It is thought that the reason for the changes in the spectra of monosubstituted succinic acids being less pronounced when the sublimation temperature is raised is that the temperature of the condensing surface is also raised, particularly when it becomes coated with a fairly thick layer of poorly heat-conducting sublimate. Then condensation at a higher temperature enables more molecules to orient themselves in the configuration stable in the solid state, *i.e.*, the " freezing " of the high-temperature equilibrium between the isomers is less complete.

The factors affecting the reconversion of the sublimed into the crystallised form can also be explained on the basis of rotational isomerisation. Of the conditions used in the present

FIG. 4.

(R = CH_3 or Cl.)

work, reconversion seems to take place most readily by way of the sodium salt in water. The acid itself in water presumably isomerises to its stable form most rapidly through its anion, and for this reason the reconversion takes place more easily in dilute than in concentrated solutions. Prevention of ionisation by the use of non-polar solvents allows the sublimed form to be heated in solution for comparatively long periods without changing its spectrum.

The stability of the two forms of methylsuccinic acid in benzene solution suggested a confirmatory test of the theory that rotational isomerisation takes place during sublimation, because it is apparent that a *gauche* isomer must have a significantly larger dipole moment than one in which the carboxyl groups are situated *trans* to each other. It is difficult to calculate with any degree of certainty how large this difference should be, as it appears from dipole measurements (Pohl, Hobbs, and Gross, *Ann. N.Y. Acad. Sci.*, 1940, **40**, 389) that even in dilute solutions such as were used in the present work, carboxylic acids are considerably associated in non-polar solvents. However, it can be expected that if one form of methylsuccinic acid has its carboxyl groups arranged *trans* to each other, its moment should be very small or zero, while a *gauche* form should, from an approximate calculation, have a dipole moment between 1·5 and 2·7 D depending upon the degree of association. The observed moments of $0{\cdot}25 \pm 0{\cdot}25$ D for crystallised and $1{\cdot}00 \pm 0{\cdot}10$ D for sublimed methylsuccinic acid are in qualitative agreement with those expected. Little significance is attached to the discrepancy between the measured dipole moment of the sublimed acid and that calculated for a *gauche* isomer, since the calculation takes no account of dipole interaction, and in addition the sublimed form must contain some of the isomer of lower moment as is indicated by its spectrum (*e.g.*, at 900 $cm.^{-1}$).

Having postulated that the presence of at least two rotational isomers is responsible for the changes produced in the infra-red spectra of methyl- and chloro-succinic acids by sublimation, we can now say something about the configurations which are present. *X*-Ray

diffraction has shown that succinic acid crystallises in long chains of centrosymmetrical molecules, the four carbon atoms of each molecule being coplanar, and the carboxyl groups being twisted out of this plane by an angle of about 10° (Morrison and Robertson, *J.*, 1949, 980; Verweel and MacGillavry, *Z. Krist.*, 1939, **102**, 60). Rieck (*Rec. Trav. chim.*, 1949, **63**, 170) found that the high-temperature form of succinic acid has the same molecular configuration but different packing of the chains. It must be concluded that the selection rules for infra-red absorption by succinic acid are considerably modified in the solid state, if the assignments of the bands at 1705 and 1720 cm.$^{-1}$ in its spectrum to symmetrical and antisymmetrical vibrations involving C=O stretching is correct. If, as the dipole measurements and infra-red spectra suggest, crystallised methyl- and chloro-succinic acids have configurations that are analogous to that of succinic acid [represented by the projection formula in Fig. 4 (*a*)] then, it being borne in mind that disubstituted succinic acids seem to show a fairly strong resistance of a carboxyl group to rotation past a β-methyl or chloro-group, the probable configuration of the unstable isomers is given in Fig. 4 (*b*). Consideration of the angles which the planes of the carboxyl groups make with say a plane perpendicular to the $C_{(2)}$–$C_{(3)}$ bond is beyond the scope of the present work.

In conclusion, it is pointed out that, when using infra-red spectra to identify compounds of this type, care must be used in preparing samples for examination if the method is not to produce confusion.

The author thanks Mr. J. F. Grove for bringing this problem to his attention and for his continued interest and help throughout the work. He is also indebted to the Directors of Imperial Chemical Industries Limited, Plastics Division, and Mr. H. A. Willis for the use of infra-red facilities, to numerous colleagues (in particular Messrs. T. A. Kletz and H. A. Willis) for helpful discussions, and to Mr. P. Jeffs for much technical assistance.

Imperial Chemical Industries Limited, Butterwick Research Laboratories,
The Frythe, Welwyn, Herts. [*Received, November 23rd*, 1951.]

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325. *Compounds containing the* 2 : 2 : 4-*Trimethylhexane Skeleton. Part II.**

By E. E. Turner and L. Turner.

The partial optical resolution of 3 : 5 : 5-trimethylhexanol is described. The (+)-form of the alcohol has been converted into the lævorotatory bromide and into (+)-2 : 2 : 4-trimethylhexane. 3 : 3 : 5-Trimethylhex-1-ene has been brominated by *N*-bromosuccinimide in the presence of benzoyl peroxide. 6-Hydroxy-2 : 2 : 4 : 9 : 11 : 11-hexamethyldodecan-7-one and 2 : 2 : 4 : 9 : 11 : 11-hexamethyldodecane-6 : 7-diol have been synthesised.

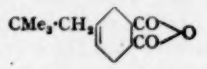
The partial optical resolution of 3 : 5 : 5-trimethylhexanol, mentioned in Part I,* has been accomplished by the fractional crystallisation, from acetone, of the brucine salt of the hydrogen phthalate. The (+)-3 : 5 : 5-trimethylhexanol obtained, when heated with hydrobromic–sulphuric acid, gave a lævorotatory bromide, the Grignard compound from which yielded (+)-2 : 2 : 4-trimethylhexane on treatment with aqueous ammonium chloride.

The product of brominating 3 : 5 : 5-trimethylhex-1-ene, $CMe_3 \cdot CH_2 \cdot CHMe \cdot CH{:}CH_2$, with *N*-bromosuccinimide in carbon tetrachloride solution in presence of benzoyl peroxide is a mixture of isomeric bromo-compounds. It reacts with *cyclo*hexylamine to give two different *cyclo*hexyltrimethylhexenylamines, isolable as the hydrochlorides in the weight ratio 8 : 1. Interaction of the mixture of bromo-compounds with sodiomalonic ester, followed by hydrolysis and decarboxylation, and then by hydrogenation, gave 5 : 7 : 7-trimethyloctanoic acid † (compare Kepner, Winstein, and Young, *J. Amer. Chem. Soc.*, 1949, **71**, 115).

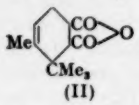
* *J.*, 1951, 2543, is considered as Part I.

† Geneva notation (CO_2H = 1) is used for long-chain acids.

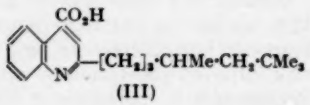
Attempts to eliminate the elements of hydrogen bromide from the monobromo-compounds led to poor yields of a 1 : 3-diolefin. The latter combines with maleic anhydride to give a product which is presumably either (I) or (II).



(I)



(II)



(III)

When heated in xylene solution under nitrogen in the presence of sodium, ethyl 3 : 5 : 5-trimethylhexanoate undergoes the acyloin condensation to give 6-hydroxy-2 : 2 : 4 : 9 : 11 : 11-hexamethyldodecan-7-one, from which 2 : 2 : 4 : 9 : 11 : 11-hexamethyldodecane-6 : 7-diol is obtained by hydrogenation.

6 : 8 : 8-Trimethylnonan-2-one (see Part I, *loc. cit.*) condenses with isatin in the presence of aqueous-alcoholic alkali, and from the product 2-(4 : 6 : 6-trimethylheptyl)quinoline-4-carboxylic acid (III) can be isolated. The constitution of this acid is proved by oxidation to quinoline-2 : 4-dicarboxylic acid. The formation of (III) is in agreement with the conclusions of Buu-Hoï (*J.*, 1946, 795; 1948, 106) that in ketones $R{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ the $CO{\cdot}CH_3$ mainly enters into formation of the quinoline ring if R is an alkyl group larger than methyl.

Experimental

Partial Resolution of 3 : 5 : 5-*Trimethylhexanol.*—A boiling solution of brucine (330 g.) and 3 : 5 : 5-trimethylhexyl hydrogen phthalate (252 g.) in acetone (550 c.c.) gave, when cooled, 141·5 g. of brucine salt. Two recrystallisations of this from the minimum of acetone gave 121 g. of salt with $[\alpha]_{5461}^{25}$ −25·6° (c = 1·6, l = 2, in chloroform). Further recrystallisations caused no change in rotation. A solution of the salt (88 g.) in acetone (700 c.c.) was poured into N-hydrochloric acid (3 l.). (+)-Trimethylhexyl hydrogen phthalate (31·5 g.) was obtained, and after recrystallisation from light petroleum (b. p. 40—60°) had m. p. 69—69·5° and $[\alpha]_{5461}^{25}$ +7·7°, +7·6°, and +7·3° (for c = 3·75, 3·00, and 2·40, respectively, l = 2, in chloroform). Hydrolysis of the ester gave (+)-3 : 5 : 5-trimethylhexanol with n_D^{25} 1·4303, d^{25} 0·8240, $[\alpha]_{5461}^{25}$ +6·7°. (−)-3 : 5 : 5-Trimethylhexyl bromide, prepared as for the (±)-compound (Part I), had b. p. 84°/21 mm., n_D^{22} 1·4528, d^{25} 1·073, $[\alpha]_{5461}^{25}$ −6·76°.

(+)-2 : 2 : 4-*Trimethylhexane.*—The Grignard solution from 17·7 g. of (−)-bromide was treated with aqueous ammonium chloride; the hydrocarbon isolated in the usual manner (40%), had n_D^{20} 1·4034, d^{25} 0·711, $[\alpha]_{5461}^{25}$ +15·2°.

Bromo-3 : 5 : 5-*trimethylhex*-1-*enes.*—Pyrolysis of 3 : 5 : 5-trimethylhexyl acetate over glass wool at 500° gave 3 : 5 : 5-trimethylhex-1-ene. A solution of the latter (251 g.), *N*-bromosuccinimide (120 g., 1 mol.), and benzoyl peroxide (1 g.) in carbon tetrachloride (200 c.c.) was stirred and boiled under reflux for 7 hours. By usual methods the bromo-olefin mixture (67·5 g., 49%) was isolated as a pale yellow, lachrymatory liquid, b. p. 46—68°/1·5 mm., n_D^{25} 1·4832 (Found: C, 53·4; H, 8·3; Br, 39·5. Calc. for $C_9H_{17}Br$: C, 52·7; H, 8·3; Br, 39·0%).

Interaction of the Bromo-olefin Mixture with cyclo*Hexylamine.*—cyclo*Hexylamine* (45 g.) was added gradually to a solution of the bromo-olefin mixture (30 g.) in 50 c.c. of anhydrous ether at 40°. *cyclo*Hexylamine hydrobromide (28 g.; m. p. 197°) was removed by filtration. The ethereal solution was extracted with water, and excess of concentrated hydrochloric acid was added to the aqueous solution. The colourless precipitate (11 g.) of mixed hydrochlorides, m. p. 162—165° (Found: C, 69·5; H, 11·6; N, 5·6; Cl, 13·3. Calc. for $C_{15}H_{30}NCl$: C, 69·3; H, 11·6; N, 5·4; Cl, 13·7%), was fractionally crystallised from light petroleum (b. p. 80—120°): 0·9 g. of a *hydrochloride*, m. p. 139—140° (Found: N, 5·25; Cl, 12·7%), and 7·6 g. of a second *hydrochloride*, m. p. 182—183° (Found: N, 5·2; Cl, 13·3%), were isolated. From the second salt excess of aqueous alkali liberated a *base*, b. p. 94°/0·5 mm., n_D^{24} 1·4737 (Found: N, 6·2. $C_{15}H_{29}N$ requires N, 6·3%).

Dehydrobromination of the Bromo-olefin Mixture.—(*a*) The bromo-compound (9 g.) was dropped on potassium hydroxide pellets at 150—200°. A distillate (1·5 g.) was obtained which, when heated in benzene with maleic anhydride, and then cooled, gave 0·35 g. of colourless leaflets, m. p. 115° [after being washed with light petroleum (b. p. 40—60°)] (Found: C, 70·2; H, 7·8. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·1%).

(*b*) The bromo-olefin mixture (24 g.), silver acetate (21 g., 1·1 mol.) and benzene (100 c.c.) were heated under reflux for 6 hours; 20·1 g. (93% yield) of a *nonenyl acetate*, b. p. 54—

56°/1 mm., n_D^{22} 1·4442—1·4460, were obtained (Found: C, 71·5; H, 11·0. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%). Pyrolysis of the acetate (18 g.) over glass wool at 490—510° gave 3·5 g. of liquid, b. p. 124—132°, n_D^{19} 1·4467—1·4508, which yielded 1·1 g. of maleic anhydride adduct, m. p. 113·5—114·5°.

Conversion of the Bromo-olefin Mixture into 5 : 7 : 7-*Trimethyloctanoic Acid.*—To sodium (2·3 g., 1 atom) and ethyl malonate (16 g., 1 mol.) in xylene (60 c.c.) at 30° were added, during 30 minutes, 20·5 g. (1 mol.) of bromo-olefin mixture. After 4 hours at 30°, followed by 3 hours at the b. p., the xylene was distilled off under reduced pressure, and the residue hydrolysed with aqueous potassium hydroxide. This gave an unsaturated acid (10·5 g., 59%), b. p. 123—125°/1 mm., n_D^{21} 1·4548—1·4558. Thereafter normal hydrogenation procedure (ethanol; PtO_2; 3—5 atm. of hydrogen) gave a 40% yield of 5 : 7 : 7-trimethyloctanoic acid, b. p. 98—99°/1 mm., n_D^{25} 1·4361. The *p*-bromophenacyl ester had m. p. 68·5°, undepressed by admixture with an authentic sample.

6-*Hydroxy*-2 : 2 : 4 : 9 : 11 : 11-*hexamethyldodecan*-7-*one.*—To a vigorously stirred mixture of sodium (4·6 g., 2 atoms) and xylene (120 c.c.) in an atmosphere of ntrogen, and at 110°, was added, during 1·5 hours, ethyl 3 : 5 : 5-trimethylhexanoate (18·6 g.). After a further 0·5 hour's heating, the product was worked up in the usual way and gave 6-*hydroxy*-2 : 2 : 4 : 9 : 11 : 11-*hexamethyldodecan*-7-*one* (12 g.), b. p. 125—133°/0·5 mm., n_D^{22} 1·4488 (Found: C, 76·2; H, 12·4. $C_{18}H_{36}O_2$ requires C, 76·0; H, 12·7%).

2 : 2 : 4 : 9 : 11 : 11-*Hexamethyldodecane*-6 : 7-*diol.*—Hydrogenation at 20°/3—5 atm. of the acyloin (36 g.), in ethyl alcohol (100 c.c.), in presence of platinum oxide, gave 2 : 2 : 4 : 9 : 11 : 11-*hexamethyldodecane*-6 : 7-*diol* (29 g., 81% yield), b. p. 122—124°/0·2 mm., n_D^{20} 1·4471 (Found: C, 76·1; H, 12·8. $C_{18}H_{38}O_2$ requires C, 75·5; H, 13·3%).

2-(4 : 6 : 6-*Trimethylheptyl*)*quinoline*-4-*carboxylic Acid.*—A mixture of isatin (4·9 g.), sodium hydroxide (7 g.), 6 : 8 : 8-trimethylnonan-2-one (5·7 g.), water (25 c.c.), and ethyl alcohol (15 c.c.) was heated at 85° for 10 hours. 6N-Hydrochloric acid (50 c.c.) was added and the precipitated 2-(4 : 6 : 6-*trimethylheptyl*)*quinoline*-4-*carboxylic acid* (8·9 g., 85%) was crystallised from 60% aqueous alcohol. The *acid* had m. p. 139·5° (softens) to 142° (Found: C 76·3; H, 8·3; N, 4·3. $C_{20}H_{27}O_2N$ requires C, 76·6; H, 8·6; N, 4·4%).

Oxidation of 2-(4 : 6 : 6-*Trimethylheptyl*)*quinoline*-4-*carboxylic Acid.*—To a solution of the acid (1·5 g.) in a solution of sodium hydroxide (10 g.) in water (45 c.c.) was added, in five portions, a solution of potassium permanganate (5 g.) in water (100 c.c.). After the mixture had been heated at 100° until the oxidation was complete, the solution was filtered and acidified, and then submitted to steam-distillation to remove aliphatic acids. The hot aqueous residual solution was filtered, and deposited on cooling a pale yellow precipitate of quinoline-2 : 4-dicarboxylic acid, m. p. 243° (Found: C, 60·1; H, 3·8. Calc. for $C_{11}H_7O_4N$: C, 60·9; H, 3·2%).

The expenses of this work were partly met by a grant from the Institute of Petroleum.

BEDFORD COLLEGE, UNIVERSITY OF LONDON. [*Received, November 30th,* 1951.]

326. *Synthesis of 3-Hydroxyisoquinolines and 2-Hydroxy-1 : 4-naphthaquinones from Esters of 2-Acyl-4 : 5-dimethoxyphenylacetic Acids.*

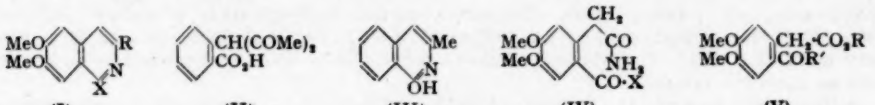
By H. R. BENTLEY, WILLIAM DAWSON, and F. S. SPRING.

Esters of 2-acetyl- and 2-benzoyl-4 : 5-dimethoxyphenylacetic acids are hydrolysed normally to the corresponding acids by aqueous sodium hydroxide, and are converted by ammonia into 3-hydroxy*iso*quinolines. With sodium hydroxide and also with aqueous ammonia, however, methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate and methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate are converted in good yield into 2-hydroxy-1 : 4-naphthaquinones.

IN the course of a search for new syntheses of papaverine (I; R = H) we have devoted some attention to the possibility of preparing 3-substituted *iso*quinolines and in particular the compounds (I; R = OH and Cl).

1 : 3-Dichloro*iso*quinoline has been obtained by the action of phosphorus oxychloride on homophthalimide (Gabriel, *Ber.*, 1886, **19**, 1653, 2354) and partial dehalogenation of the former is stated to give 3-chloro*iso*quinoline; 1-chloro-3-hydroxy*iso*quinoline is also obtained by partial reaction of homophthalimide (Gabriel, *loc. cit.*). Apart from these

examples, so far as we are aware, 3-chloro- and 3-hydroxy-*iso*quinolines have not been described. A possible route to the 3-hydroxy*iso*quinolines was suggested by the work of Hurtley (*J.*, 1929, 1870) who showed that evaporation of an aqueous solution of the ammonium salt of the keto-acid (II) gave 1-hydroxy-3-methyl*iso*quinoline (methyl*iso*carbostyril) (III). With the ultimate object of effecting a synthesis of papaverine *via* 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetamide (IV) a general study of the preparation and properties of derivatives of 2-acyl-4 : 5-dimethoxyphenylacetic acids (V; R = H) was undertaken.



(I) (II) (III) (IV) (V)

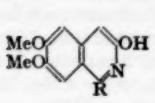
[X = 3 : 4 : 1-$(MeO)_2C_6H_3$·CH_2·]

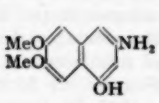
In preliminary experiments, ethyl homoveratrate and acetyl chloride were found to react smoothly with aluminium chloride in carbon disulphide, to give ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (V; R = Et, R′ = Me). By using methyl homoveratrate the corresponding methyl ester was obtained. The orientation of the acetyl group in these two esters was established by oxidation with sodium hypochlorite which in each case gave 2-carboxy-4 : 5-dimethoxyphenylacetic acid (V; R = H, R′ = OH). Previous application of the Friedel–Crafts ketone synthesis to the phenylacetic acid series is confined to ethyl phenylacetate itself which with chloroacetyl chloride gives ethyl *p*-chloroacetylphenylacetate (Kunckell, *Ber.*, 1905, **38**, 2610). Ethyl and methyl 2-acetyl-4 : 5-dimethoxyphenylacetates (V; R = Et and Me; R′ = Me) are hydrolysed normally by aqueous sodium hydroxide to the acid (V; R = H, R′ = Me). Each of the esters reacts with aqueous ammonia to give, in good yield, a product $C_{12}H_{13}O_3N$, apparently by formation of the corresponding amide followed by loss of the elements of water. Attempts to isolate the intermediate amide were unsuccessful. This compound has been shown to be 3-hydroxy-6 : 7-dimethoxy-1-methyl*iso*quinoline (VI; R = Me) and the alternative formulation as 3-amino-6 : 7-dimethoxy-1-naphthol (VII) has been excluded by the following facts. The compound forms a crystalline picrate and hydrochloride and gives an intense red-violet ferric chloride colour; it does not react with nitrous acid and is converted by acetic anhydride into a monoacetate which, since it does not give a ferric chloride colour, is an *O*-acetate. The 3-hydroxy*iso*quinoline structure is confirmed by preparation of 3-hydroxy-6 : 7-dimethoxy-1-phenyl*iso*quinoline (VI; R = Ph) from methyl 2-benzoyl-4 : 5-dimethoxyphenylacetate (V; R = Me, R′ = Ph). The last-named compound is also hydrolysed normally by aqueous sodium hydroxide but fails to react with aqueous ammonia at ordinary temperatures. It is converted into 3-hydroxy-6 : 7-dimethoxy-1-phenyl*iso*quinoline (VI; R = Ph) by ethanolic ammonia at 130—140°; in this case, cyclisation by the alternative route to give an aminophenol is excluded.

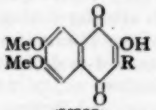
The two 3-hydroxy*iso*quinolines described above are high-melting yellow compounds with phenolic properties: they are soluble in aqueous sodium hydroxide, give violet ferric chloride colours, and form red azo-derivatives with benzenediazonium chloride solution. It has not been possible to replace the 3-hydroxyl group by chlorine by using phosphorus oxychloride (cf. Gabriel, *loc. cit.*; Gabriel and Colman, *Ber.*, 1900, **33**, 985). 3-Hydroxy*iso*quinolines are thus more truly phenolic than are 1-hydroxy*iso*quinolines and resemble 3-hydroxy-pyridines and -quinolines rather than the formally analogous 2-hydroxy-derivatives.

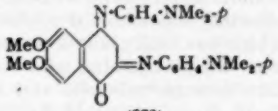
In attempts to extend these reactions to the phenylacetyl series, methyl homoveratrate reacted smoothly also with phenylacetyl chloride, giving methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) which was not hydrolysed normally in aqueous sodium hydroxide and did not yield a 3-hydroxy*iso*quinoline with ammonia. Both of these reagents convert the keto-ester smoothly and in good yield into bright-red 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone (VIII; R = Ph) [neither the carboxylic acid (V; R = H; R′ = CH_2Ph) nor the corresponding amide could be isolated].

This quinone gives a monoacetate, a monobenzoate, and a monomethyl ether, and on reductive acetylation furnishes the corresponding triacetoxynaphthalene derivative. Similarly treatment of methyl homoveratroyl chloride gives methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate [V; R = Me, R′ = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$] which with either aqueous sodium hydroxide or ammonia gives 2-hydroxy-6 : 7-dimethoxy-3-(3 : 4-dimethoxyphenyl)-1 : 4-naphthaquinone [VIII; R = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$]. Although ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (V; R = Et,


(VI)


(VII)


(VIII)


(IX)

R′ = Me) reacts normally with aqueous sodium hydroxide to give the corresponding carboxylic acid and does not yield a naphthaquinone under these conditions, the ketone is rapidly converted into 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (VIII; R = H) in good yield by ethanolic sodium ethoxide with free access to air.

The formation of 2-hydroxynaphthaquinones from alkyl 2-acylphenylacetates proceeds by intramolecular loss of ethanol or water to give a 1 : 3-dihydroxynaphthalene, atmospheric oxidation of which will proceed rapidly in alkaline solution to give the corresponding hydroxynaphthaquinone (cf. Volhard, *Annalen*, 1897, **296**, 14; Soliman and Latif, *J.*, 1944, 55). In support of this view, treatment of methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) with sodium ethoxide and ethanol with complete exclusion of oxygen gave a colourless amorphous phenolic product which oxidised rapidly to the corresponding red hydroxynaphthaquinone on exposure to the air.

The structures assigned to the 2-hydroxynaphthaquinones (VIII; R = H and Ph) have been confirmed by unambiguous syntheses which also serve to establish the assumed orientation of the substituent groups in methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) and hence, by analogy, that of the groups in the keto-ester [V; R = Me, R′ = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$]. Condensation of 6 : 7-dimethoxy-1-tetralone with *p*-nitrosodimethylaniline gives the anil (IX), hydrolysis of which gives 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (VIII; R = H) identical with the specimen obtained by the route described above (cf. Pfeiffer and Hesse, *J. pr. Chem.*, 1941, **158**, 315). Treatment of the last compound with benzenediazonium chloride (cf. Neunhoeffer and Weise, *Ber.*, 1938, **71**, 2705) gave 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone identical with the compound obtained as described above.

Experimental

**Ethyl 2-Acetyl-4 : 5-dimethoxyphenylacetate.*—Dry, finely powdered aluminium chloride (12·0 g., 1 mol.) and acetyl chloride (6·4 ml., 1 mol.) were added to a cooled solution of ethyl homoveratrate (20·0 g., 1 mol.) in dry carbon disulphide (120 ml.). The mixture was boiled under reflux for 1 hour, then cooled, and the solvent decanted from the dark complex which was decomposed with ice-water. The product was collected by means of ether, and the ethereal extract washed with saturated aqueous sodium hydrogen carbonate and then with water, dried, and evaporated, to give *ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate* (12·0 g., 51%) which crystallises from light petroleum (b. p. 60—80°) as silky needles, m. p. 94° (Found: C, 63·3; H, 6·6. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%), and gives a red *2 : 4-*dinitrophenylhydrazone*, rhombs (from ethyl acetate), m. p. 171° (Found: C, 53·6; H, 4·9. $C_{20}H_{22}O_8N_4$ requires C, 53·8; H, 5·0%).

Methyl 2-Acetyl-4 : 5-dimethoxyphenylacetate.—This *ester* (3·5 g., 30%) was obtained similarly from methyl homoveratrate (9·5 g.), acetyl chloride (3·5 g.), and aluminium chloride (6·0 g.) in carbon disulphide (60 ml.) and after crystallisation from ether–light petroleum (b. p. 60—80°) formed needles, m. p. 114° (Found: C, 61·7; H, 6·7. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4%). The 2 : 4-*dinitrophenylhydrazone* separated as red needles, m. p. 194°, from ethyl acetate (Found: N, 13·7. $C_{19}H_{20}O_8N_4$ requires N, 13·0%).

* We are grateful to Professor Sir Robert Robinson, F.R.S., for permission to include a description of the compounds thus marked, which were first made in the Oxford laboratory (H. R. Bentley, Thesis, 1947).

**2-Acetyl-4 : 5-dimethoxyphenylacetic Acid.*—Hydrolysis of the methyl and the ethyl ester with aqueous sodium hydroxide (5%), by either shaking overnight at room temperature or boiling for 15 minutes under reflux followed by acidification, gave *2-acetyl-4 : 5-dimethoxyphenylacetic acid* which crystallised from ethanol as needles, m. p. 175° (Found: C, 60·3; H, 6·1. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%).

2-Carboxy-4 : 5-dimethoxyphenylacetic Acid.—Methyl 2-acetyl-4 : 5-dimethoxyphenylacetate (150 mg.) was hydrolysed by aqueous sodium hydroxide (10%, 10 ml.) at 80° during 15 minutes. Sodium hypochlorite solution [6·0 ml.; from aqueous sodium hydroxide (20%) saturated with chlorine] was added dropwise with stirring during 30 minutes to the cooled alkaline solution which was finally boiled under reflux for 15 minutes. After cooling of the solution and acidification, the precipitated solid was collected and crystallised from water, to yield 2-carboxy-4 : 5-dimethoxyphenylacetic acid as needles, m. p. 216° (Found: C, 55·3; H, 5·3. Calc. for $C_{11}H_{12}O_6$: C, 55·0; H, 5·0%) (Perkin and Robinson, *J.*, 1907, **91**, 1082, give m. p. 215°).

**3-Hydroxy-6 : 7-dimethoxy-1-methylisoquinoline.*—Finely powdered ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (1·0 g.) was shaken for 16 hours with aqueous ammonia (*d* 0·88; 30 ml.); the yellow solid (0·5 g., 60%) was collected and crystallised from ethanol, giving *3-hydroxy-6 : 7-dimethoxy-1-methylisoquinoline* as yellow prisms, m. p. 286° (decomp.) (Found: C, 65·7; H, 6·0; N, 6·6. $C_{12}H_{13}O_3N$ requires C, 65·7; H, 5·9; N, 6·4%). This does not react with nitrous acid, but in ethanol yields a *picrate* which crystallises from ethanol as yellow prisms, m. p. 236—239° (Found: C, 48·3; H, 3·4. $C_{12}H_{13}O_3N,C_6H_3O_7N_3$ requires C, 48·2; H, 3·6%). Addition of excess of hydrochloric acid to a solution of the base in aqueous sodium hydroxide gives a *hydrochloride*, crystallising from aqueous dioxan as pale yellow needles, m. p. 250° (decomp.) after softening from 240° (Found: C, 52·7; H, 5·8; N, 5·4. $C_{12}H_{13}O_3N,HCl,H_2O$ requires C, 52·65; H, 5·9; N, 5·1%); the base is recovered from the hydrochloride by treatment with aqueous sodium hydrogen carbonate. The base (0·1 g.) and boiling acetic anhydride (3·0 ml.) give in 1 hour a *monoacetate*, crystallising from light petroleum (b. p. 60—80°)–benzene as needles, m. p. 139—140° (Found: C, 64·6; H, 5·7; N, 5·8. $C_{14}H_{15}O_4N$ requires C, 64·35; H, 5·8; N, 5·4%).

Methyl 2-Benzoyl-4 : 5-dimethoxyphenylacetate.—Dry, finely powdered aluminium chloride (9·0 g., 1·3 mols.) and benzoyl chloride (9·4 g., 1·3 mols.) were added to methyl homoveratrate (10·0 g., 1·0 mol.) in dry carbon disulphide (150 ml.), and the mixture was boiled under reflux for 2 hours. Solvent was then decanted from the dark complex which was allowed to decompose for several hours in contact with ice-water. The product was isolated with ether, the ethereal solution washed with saturated sodium carbonate solution, and the dried solution evaporated. The residue crystallised partly after several hours in the refrigerator. The solid was collected (5·1 g., 34%) by using a small volume of cold ethanol, and crystallised from benzene–light petroleum (b. p. 60—80°), giving *methyl 2-benzoyl-4 : 5-dimethoxyphenylacetate* as stout needles, m. p. 107° (Found: C, 68·8; H, 5·6. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%).

Hydrolysis for 30 minutes in boiling aqueous sodium hydroxide (10%) followed by acidification gave the *acid* which crystallised from aqueous ethanol as long needles, m. p. 163° (Found: C, 67·6; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

3-Hydroxy-6 : 7-dimethoxy-1-phenylisoquinoline.—A mixture of methyl 2-benzoyl-4 : 5-dimethoxyphenylacetate (1·0 g.) and saturated ethanolic ammonia (30 ml.) was heated at 130—140° for 4 hours in the autoclave. Evaporation of the solvent gave a partly crystalline product which was collected with ethanol. *3-Hydroxy-6 : 7-dimethoxy-1-phenylisoquinoline* (550 mg., 61%) crystallised from ethanol as yellow prisms, m. p. 243° (decomp.) after softening from 230° (Found: C, 72·2; H, 5·5; N, 5·3. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·4; N, 5·0%).

Methyl 4 : 5-Dimethoxy-2-phenylacetylphenylacetate.—A mixture of methyl homoveratrate (20·0 g.), dry powdered aluminium chloride (12·8 g., 1 mol.) and phenylacetyl chloride (14·8 g., 1 mol.) in dry carbon disulphide (120 ml.) was boiled under reflux for 1 hour, then cooled, and the solvent decanted from the dark complex which was then decomposed with ice-water. The product was collected by means of ether, giving *methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate* (10·0 g., 32%) which crystallised from chloroform–light petroleum (b. p. 60—80°) as needles, m. p. 94° (Found: C, 69·8; H, 6·2. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%), and gave a 2 : 4-*dinitrophenylhydrazone* crystallising from ethanol as red needles, m. p. 148° (Found: N, 10·8. $C_{25}H_{24}O_8N_4$ requires N, 11·0%).

Methyl 4 : 5-Dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate.—Homoveratroyl chloride (7·0 g.) was added to an ice-cold solution of powdered aluminium chloride (7·0 g.) in nitrobenzene (50 ml.), and methyl homoveratrate (10·0 g.) was added dropwise with stirring during 1 hour. The mixture was stirred overnight at room temperature, ether (100 ml.) was added and sufficient

crushed ice to decompose the complex. The ethereal layer was separated, washed with dilute hydrochloric acid, saturated sodium hydrogen carbonate solution, and water, and freed from solvents by steam-distillation. The product was collected by means of benzene and crystallised from benzene–light petroleum (b. p. 60—80°), to give *methyl* 4 : 5-*dimethoxy*-2-(3 : 4-*dimethoxyphenylacetyl*)*phenylacetate* (1·7 g., 13%) as rosettes of prisms, m. p. 132° (Found : C, 65·2; H, 6·5. $C_{21}H_{24}O_7$ requires C, 64·9; H, 6·2%). The 2 : 4-*dinitrophenylhydrazone* crystallises from ethanol as red needles, m. p. 150° (Found : C, 57·3; H, 5·2. $C_{27}H_{28}O_{10}N_4$ requires C, 57·0; H, 5·0%).

2-*Hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone*.—Methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (200 mg.) was shaken with sodium hydroxide solution (5%; 10 ml.) or with aqueous ammonia (*d* 0·88; 10 ml.) during 2 days. The deep violet solution was acidified and the precipitated solid (100 mg., 53%) crystallised from methanol–chloroform, to give 2-*hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone* as long red needles, m. p. 255° (Found : C, 70·0; H, 4·8. $C_{18}H_{14}O_5$ requires, C, 69·7; H, 4·5%). This gives a red-brown colour (not intense) with ferric chloride in ethanol and a dark-green colour with concentrated sulphuric acid. With acetic anhydride in pyridine it forms a *monoacetate* which crystallises from chloroform–methanol as microscopic yellow prisms, m. p. 218—220° (Found : C, 68·2; H, 4·8. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·6%). With benzoyl chloride in pyridine a *monobenzoate* is obtained which crystallises from chloroform–methanol as orange prisms, m. p. 232° (Found : C, 72·4; H, 4·6. $C_{25}H_{18}O_6$ requires C, 72·4; H, 4·4%). With an excess of ethereal diazomethane the 2-hydroxynaphthaquinone gives 2 : 6 : 7-*trimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone* which crystallises from chloroform–methanol as microscopic yellow prisms, m. p. 214° (Found : C, 70·0; H, 5·1. $C_{19}H_{16}O_5$ requires C, 70·4; H, 5·0%). A solution of the quinone (300 mg.) in acetic anhydride (5 ml.) containing zinc dust (300 mg.) and sulphuric acid (*d* 1·84; 0·1 ml.) was boiled under reflux for 20 minutes; the solution was decanted from solid and decomposed with water. The solid product (250 mg., 60%) separating overnight was collected and crystallised from ethanol, to give 1 : 2 : 4-*triacetoxy*-6 : 7-*dimethoxy*-3-*phenylnaphthalene* as clusters of stout needles, m. p. 175—177° (Found : C, 66·0; H, 5·1. $C_{24}H_{22}O_8$ requires C, 65·75; H, 5·1%).

2-*Hydroxy*-6 : 7-*dimethoxy*-3-(3 : 4-*dimethoxyphenyl*)-1 : 4-*naphthaquinone*.—Treatment of methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate with aqueous sodium hydroxide or ammonia as described above gives 2-*hydroxy*-6 : 7-*dimethoxy*-3-(3 : 4-*dimethoxyphenyl*)-1 : 4-*naphthaquinone* which crystallises from methanol as long red needles, m. p. 226° (Found : C, 65·0; H, 5·1. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%). The *monobenzoate* was obtained as orange prisms, m. p. 206°, from chloroform–methanol (Found : C, 68·3; H, 4·4. $C_{27}H_{22}O_8$ requires C, 68·3; H, 4·7%).

2-*Hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone*.—(*a*) Solutions of 6 : 7-dimethoxy-1-tetralone (5·2 g., 1 mol.) in ethanol (50 ml.) and *p*-nitrosodimethylaniline (7·5 g., 2 mols.) in ethanol (100 ml.) together with aqueous sodium hydroxide (10%; 5 ml.) were mixed and set aside at room temperature. Next day the precipitate (5·5 g., 46%) was collected and crystallised from ethyl acetate, to give 1 : 2 : 3 : 4-*tetrahydro*-1-*keto*-6 : 7-*dimethoxy*-2 : 4-*bis*-p-*dimethylanilonaphthalene* as small permanganate-coloured needles, m. p. 230° (decomp.) (Found : C, 71·2; H, 6·2; N, 11·9. $C_{28}H_{30}O_2N_4$ requires C, 71·5; H, 6·4; N, 11·9%). A mixture of the anil (10·0 g.) and sulphuric acid (20% w/v; 300 ml.) was boiled under reflux for 1 hour, then cooled, and the solid product was collected, dried *in vacuo*, and extracted (charcoal) with boiling benzene (2 × 500 ml.). Concentration of the combined extracts gave 2-*hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone* (800 mg., 16%), which was obtained after recrystallisation from benzene and sublimation (10^{-3} mm.) as microscopic orange needles, m. p. 212° (decomp.) (Found : C, 61·4; H, 4·5. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%).

(*b*) Solutions of ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (1·0 g.) in ethanol (30 ml.) and of sodium (0·18 g., 2 atoms) in ethanol (5 ml.) were mixed and the mixture was boiled under reflux for 20 minutes and set aside at room temperature with free access to air. Next day the red solid was collected, washed with ethanol, dried, and dissolved in water (50 ml.). Acidification of the aqueous solution gave an orange-brown precipitate (700 mg., 80%) which was collected, washed with water and ethanol, dried, and crystallised from benzene, giving 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone as small orange needles, m. p. 212° (decomp.) alone or mixed with the specimen described above.

2-*Hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone from* 2-*Hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone*.—Aniline (290 mg.) in water (12 ml.) and hydrochloric acid (*d* 1·18; 0·36 ml.) was diazotised at 0° with sodium nitrite (250 mg.) in water (5 ml.) and hydrochloric acid (*d* 1·18; 0·36 ml.). The solution was added dropwise with stirring during 5 minutes to a solution of

2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (560 mg.) in potassium hydroxide solution (5%; 24 ml.) kept at 45°. After a further 20 minutes' stirring at 45° the mixture was adjusted to pH 6·0 with dilute acetic acid and filtered. The filtrate was acidified with hydrochloric acid, and the yellow precipitate collected, washed, and dried (150 mg.). Crystallisation from ethanol gave a red-orange solid (50 mg.), m. p. 240°, which after chromatography on calcium carbonate with benzene as solvent gave 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone (20 mg.), crystallising from methanol–chloroform as red needles, m. p. 255°, alone or mixed with a sample prepared by the alternative route.

We are grateful to Messrs. T. and H. Smith, Ltd., Edinburgh, for the gift of a number of chemicals, and one of us (W. D.) thanks the Department of Scientific and Industrial Research for a Maintenance award.

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THE ROYAL TECHNICAL COLLEGE, GLASGOW.
THE DYSON PERRINS LABORATORY, OXFORD. [*Received, January 14th*, 1952.]

327. *Hydroaromatic Steroid Hormones. Part III.* Some Angular-methylated Intermediates.*

By A. J. BIRCH, J. A. K. QUARTEY, and HERCHEL SMITH.

An attempt to introduce an angular methyl group into the 4-methylanilinomethylene derivative of 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxychrysene (IV) gave 1 : 2-dihydro-3 : 10-dimethoxy-4-*N*-methylanilinomethylchrysene (VI), but the direct methylation of 1 : 2 : 3 : 4 : 5 : 8-hexahydro-1-keto-6-methoxynaphthalene (IX) produced 1 : 2 : 3 : 4 : 8 : 9-hexahydro-1-keto-6-methoxy-9-methylnaphthalene (XI), an important intermediate in steroid synthesis. Further reactions led to the 1-hydroxy-6-keto-9-methyl compound. Similar angular methylation of 4 : 7-dihydro-5-methoxyindan-1-one was achieved.

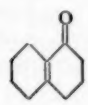
THE reduction of aromatic systems by alkali metals and alcohols in liquid ammonia, which has been used so far in this series in attempts to synthesise biologically active analogues of steroid hormones, leads readily to the 19-nor-steroid hormones, 19-nortestosterone † and 19-norprogesterone, which have high hormone activity (Birch, *J.*, 1950, 367; Birch and Smith, Part II *; Miramontes, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 3540). However, the method cannot lead directly, by the reduction of aromatic rings, to compounds containing angular methyl groups, and some exploratory work has been carried out on the introduction of these groups into compounds accessible by means of the reduction reactions.

Preliminary work on an indirect route for the introduction of the $C_{(10)}$-Me into the 19-nortestosterone indicates that, although probably feasible, it is not likely to be of practical importance (Birch, *Chem. and Ind.*, 1951, 616). Accordingly, methods for the direct introduction of a methyl group into octahydroketonaphthalene derivatives of type (I) are now being explored, on the basis of theoretical ideas on the conversion of αβ- into βγ- unsaturated ketones which have already been outlined (Birch, *J.*, 1950, 1551) and have been successfully exploited in the conversion of cholest-4-en-3-one into cholest-5-en-3-one (Birch, *J.*, 1950 2523). Briefly, if compounds of type (I) can be converted into salts containing mesomeric anions of type (II), then the action of methyl iodide on these salts may be expected to lead chiefly to compounds of type (III). It is probable that the requisite salts may in some cases be directly produced by the action of the correct enolising agent; in other cases indirect routes may be necessary, *e.g.*, through enol esters (cf. *loc. cit.*). This aspect is being examined.

Preparation of the chrysene ketone (IV) was reported in Part II of this series, and its conversion into (V) would constitute a synthesis of (±)-D-homoequilenin, because hydrogenation of the double bond has been shown to give the correct *trans*-linkage of the C–D rings (Burnop, Elliott, and Linstead, *J.*, 1940, 727; Bachmann and Holmes, *J. Amer. Chem.*

* Part II, *J.*, 1951, 1882.
† Formerly called 10-nortestosterone. For the present nomenclature see *J.*, 1951, 3526.

Soc., 1941, **63**, 2592) : direct angular methylation of 1-ketodecalin derivatives, on the other hand, leads predominantly to the unwanted *cis*-isomer (*e.g.*, Birch and Robinson, *J.*, 1944, 501). In order to prevent enolisation in its direction, the 4-methylene group was protected as the *N*-methylanilinomethylene derivative (Birch and Robinson, *J.*, 1944,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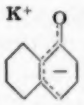
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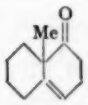
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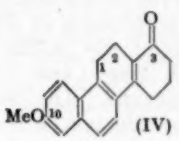
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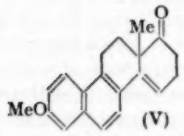
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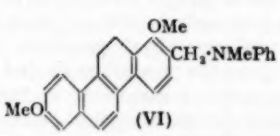
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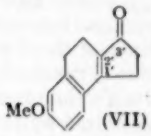

(VII)

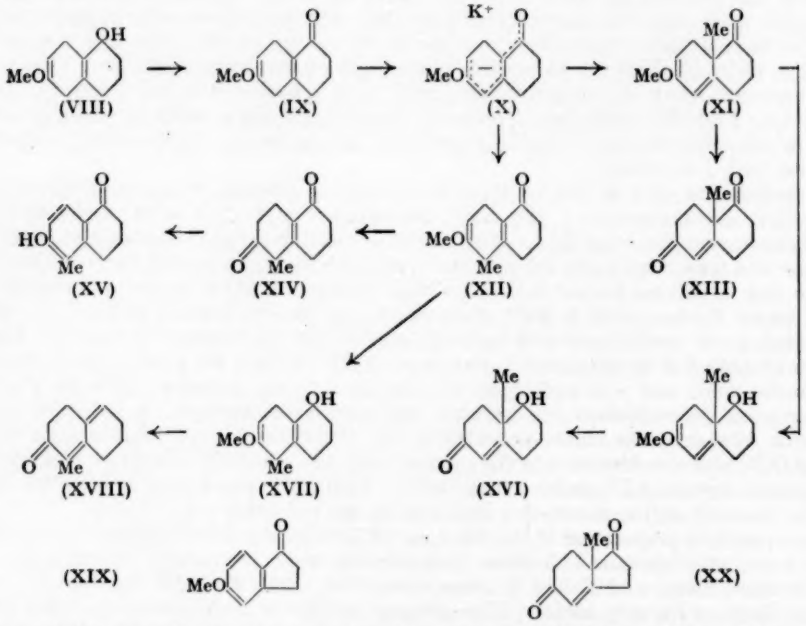
510). This with potassium *tert.*-butoxide and methyl iodide gave a colourless base which did not lose its nitrogen on acidic or alkaline hydrolysis and appeared to be (VI), formed by bond-migration and methylation. Now, with a five-membered D-ring such aromatisation is impossible. Accordingly, (VII) was synthesised by the general method of Johnson, Johnson, and Petersen (*J. Amer. Chem. Soc.*, 1945, **67**, 1360). Its methylanilinomethylene derivative gave after the methylation procedure and hydrolysis only impure starting material in poor yield. Introduction of the methyl group by this procedure is therefore not easy, although it should be possible in the right experimental conditions. Since this work was completed, Woodward, Sondheimer, Taub, Heusler, and McLamore (*J. Amer. Chem. Soc.*, 1951, **73**, 2403) have reported a closely analogous reaction in which a carbon atom becomes quaternary, a similarly protected αβ-unsaturated ketone being caused to condense with acrylonitrile.

Attention was then turned to what, on theoretical grounds, was considered to be a particularly favourable case : the direct methylation of 1 : 2 : 3 : 4 : 5 : 8-hexahydro-1-keto-6-methoxynaphthalene (IX). This was expected to form a salt readily because it can give rise to a fully conjugated anion of the type (X) by loss of a proton from the dihydroanisole ring, a process known to be easy with potassium amide in liquid ammonia (cf. Birch, *Quart. Reviews*, 1950, **4**, 69). According to the results obtained by Birch (*J.*, 1950, 1551) such a salt should react with methyl iodide to give the methoxy-ketone (XI) with a smaller likelihood of the formation of its isomer (XII). In fact, the chief product obtained after methylation and acid hydrolysis was identified as the diketone (XIII) by a mixed melting point determination and infra-red and ultra-violet spectra. A specimen of the authentic substance was kindly provided by Dr. R. H. Jaeger. A small amount of the phenol (XV) was also identified in the product, and was evidently formed by oxidation of the unstable ketone (XIV) derived from (XII). That (XII) was formed in some 10—15% yield in the methylation was further indicated by the reduction results below.

As a practical preparation of the diketone (XIII) the method is unlikely to rival that from 2-methyl*cyclo*hexane-1 : 3-dione (unpublished work in various laboratories; cf. also Wendler, Slates, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 3816), but the enol ether (XI) is likely to be very useful. The structure of this is confirmed by its ultra-violet absorption maximum at 274 mμ (ε 5200) with an inflexion at 241 mμ (ε 4450). It contains a grouping readily convertible by acid hydrolysis into that found in the A–B rings of physiologically active hormones such as testosterone, progesterone, and cortisone; for the potential carbonyl group in the steroid 3-position is protected as the enol ether against anionoid reagents, while the other carbonyl group is in the right position to facilitate the addition of rings C and D. Furthermore, (XI) is a potential starting material for rings C–D of D-homosteroids and ring-opened analogues. Its reduction with lithium aluminium hydride followed by acid hydrolysis produced the keto-alcohol (XVI) and, as by-product, the dienone (XVIII) formed from (XII) (present as impurity) by reduction to (XVII) and dehydration

during acid hydrolysis (cf. Birch, *J. Proc. Roy. Soc., N.S.W.*, 1950, **83**, 245). The steric configuration of the hydroxyl group has not been ascertained. It may be β by analogy with the reduction of 17-ketosteroids, but Heusser, Wahba, and Herzig (Abs. 120th Meeting Amer. Chem. Soc., 1951, 9L) have shown that 17a-keto-D-homo-steroids do not necessarily obey the rule of α-attack of a reagent.

The preparation of (IX) was based on the 6 : 8-reduction, already described (Birch, *loc. cit.*), of the readily available 1 : 2 : 3 : 4-tetrahydro-1-keto-6-methoxynaphthalene (Stork, *J. Amer. Chem. Soc.*, 1947, **69**, 576) to (VIII) by means of sodium and ethanol in liquid ammonia. The yield has been raised to 55%, and it is clear from unpublished work that prior reduction of the carbonyl group with a milder reagent would further improve this yield by largely eliminating the reductive removal of methoxyl, which is a side-reaction. The principal loss is due to hydrogenolysis of the hydroxyl group, and it may be noted that in absence of the "*p*"-methoxyl group hydrogenolysis is complete. An Oppenauer-type oxidation of the alcohol (VIII) gave the crystalline ketone (IX), the structure of which is in accord with the ultra-violet absorption maximum at 238 mμ. The reduced benzene ring was unaffected by this structure-specific oxidation process, despite the extreme sensitivity of (VIII) and (IX) to the usual oxidising agents and to air. In order to avoid the reduction and re-oxidation of the carbonyl group attempts were made to protect this as the acetal, following the successful reduction of the ring in anisaldehyde when this method of protection is used. However, all efforts to prepare cyclic or acyclic acetals by standard methods failed.



As a further application of the general angular-methylation procedure, 5-methoxyindan-1-one (XIX) was converted by the same stages into the diketone (XX) in rather poor yield. Extensions of the process are being investigated.

Experimental

1 : 2 : 3 : 4 : 5 : 6-*Hexahydro*-3-*keto*-10-*methoxy*-4-N-*methylanilinomethylenechrysene*.—Ethyl formate (3·75 c.c.) in benzene (3·75 c.c.) was added under nitrogen to dry sodium methoxide (from the metal, 0·54 g.) and, after 15 minutes, 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxychrysene (1·06 g.) in benzene (15 c.c.) was added. The mixture was shaken occasionally and

left overnight. After the addition of water (5 c.c.) and a little ice, the sparingly soluble yellow sodium salt was filtered off and washed with benzene, followed by a little alcohol and ether. Acetic acid (10 c.c.) and water (90 c.c.) liberated the formyl compound as a buff-coloured solid (1·0 g.) which gave a deep purple colour with ferric chloride. The crude substance (1·0 g.), benzene (50 c.c.), and methylaniline (0·5 g.) were refluxed in the presence of anhydrous sodium sulphate for 30 minutes and then filtered. Evaporation of the solvent under reduced pressure left a brownish resin which was repeatedly extracted with boiling light petroleum (b. p. 40—60°) containing 5% of benzene. Concentration of the extract to *ca.* 30 c.c. gave a crystalline solid which was recrystallised from tetrahydrofuran–ethanol (1 : 1), to give 1 : 2 : 3 : 4 : 5 : 6-*hexahydro*-3-*keto*-10-*methoxy*-4-N-*methylanilinomethylenechrysene* (0·75 g.) as yellow needles, m. p. 183° (Found : C, 81·9; H, 6·0; N, 3·8. $C_{37}H_{33}O_2N$ requires C, 82·0; H, 6·3; N, 3·5%).

1 : 2-*Dihydro*-3 : 10-*dimethoxy*-4-N-*methylanilinomethylchrysene*.—The above compound (0·75 g.) in tetrahydrofuran (20 c.c.) was added to a solution of potassium (0·7 g.) in *tert.*-butanol (20 c.c.) under nitrogen. The mixture was refluxed for 5 minutes and methyl iodide added to the boiling solution to discharge the brown colour. Water (30 c.c.) was added. The oily precipitate rapidly crystallised to aggregates of needles. The product was purified by passage in benzene through alumina (50 g.). Crystallisation from benzene–methanol (1 : 1) gave 1 : 2-*dihydro*-3 : 10-*dimethoxy*-4-N-*methylanilinomethylchrysene* (0·52 g.) as long white needles, m. p. 144—145° (Found : C, 81·8; H, 6·7; N, 3·5. $C_{38}H_{37}O_2N$ requires C, 82·2; H, 6·6; N, 3·4%). The compound was soluble in concentrated hydrochloric acid and was recovered unchanged after 3 hours in a boiling mixture of ethanol (14 c.c.), water (3 c.c.), and sulphuric acid (1 c.c.). Attempted methylation of the unprotected hexahydroketomethoxychrysene under the same conditions resulted in recovery of most of the starting material.

3 : 4-*Dihydro*-3′-*keto*-6-*methoxy*cyclo*penteno*(1′ : 2′-1 : 2)*naphthalene*.—1 : 2 : 3 : 4-Tetrahydro-1-keto-6-methoxynaphthalene (17·6 g.) and methyl succinate (21·9 g.) were added (in nitrogen) to a chilled solution of potassium (4·3 g.) in *tert.*-butanol (80 c.c.), and the light orange suspension was heated under reflux for 90 minutes. On cooling, the mixture was acidified and the solvents were removed under reduced pressure, to give an oily residue which was taken up in ether and washed with water. The washings were re-extracted with ether. The combined ethereal extracts were extracted thoroughly with saturated sodium hydrogen carbonate solution, and the extract was acidified. The pink oil was taken up in ether, washed with water, dried, and evaporated, to leave a golden-brown viscous oil which failed to crystallise. This product (6 g.) in acetic anhydride (60 c.c.) was added to fused zinc chloride (0·6 g.) in acetic acid (30 c.c.), and the whole refluxed under nitrogen for 3 hours. Excess of anhydride was decomposed by cautious addition of water (60 c.c.), concentrated hydrochloric acid (24 c.c.) was added, and refluxing continued until the evolution of carbon dioxide had ceased (3 hours). The solvents were removed under reduced pressure and the dark residue was heated on the steam-bath for 40 minutes with aqueous potassium hydroxide (5%). The residual oil was taken up in ether–ethyl acetate (1 : 1), and the solvent evaporated under reduced pressure. The residue was repeatedly extracted with boiling light petroleum (b. p. 40—60°), and the crystalline compound obtained by concentration of the extracts purified by passage in benzene–light petroleum (b. p. 60—80°) (2 : 1) through alumina (20 g.). Crystallisation from benzene–light petroleum (b. p. 60—80°) (1 : 1) gave 3 : 4-*dihydro*-3′-*keto*-6-*methoxy*cyclo*penteno*(1′ : 2′-1 : 2)*naphthalene* as pale yellow needles (1·1 g.), m. p. 96—97° (Found : C, 78·8; H, 6·2. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). It had bands in the ultra-violet at 329 (ε = 23,960 and 238 mμ ε = 12,270), in accord with the assigned structure. The 2 : 4-dinitrophenylhydrazone separated from ethyl acetate as dark purple-red needles, m. p. 275°. Unchanged methoxytetralone (14 g.) was recovered, and the total amount of product obtained was 2·5 g. or 57% based on the methoxytetralone consumed. Oxidation with hot aqueous permanganate gave as the only recognisable product succinic acid, m. p. 184°.

3 : 4-*Dihydro*-3′-*keto*-6-*methoxy*-4′-N-*methylanilinomethylene*cyclo*penteno*(1′ : 2′-1 : 2)*naphthalene*.—Ethyl formate (7·5 c.c.) in benzene (7·5 c.c.) was added under nitrogen to pure dry sodium methoxide (from the metal, 1·02 g.) and, after 15 minutes, the above ketone (1·5 g.) in benzene (10 c.c.) was added. The deep yellow mixture was shaken occasionally during 1 hour and then left for 18 hours and worked up as for the formyl compound above, to give a yellow solid (1·4 g.) producing an intense purple colour with ferric chloride. A solution of this in benzene with methylaniline (1·5 g.) was refluxed for 1 hour under nitrogen in the presence of anhydrous sodium sulphate. Worked up as above, the *methylanilinomethylene* compound (1·0 g.) crystallised from ethyl acetate as orange-yellow needles, m. p. 139—140° (Found : N, 4·2. $C_{22}H_{21}O_2N$ requires N, 4·2%). The compound (0·3 g.) in *tert.*-butanol (15 c.c.) was added to a solution of potassium

(0·38 g.) in *tert.*-butanol (10 c.c.) under nitrogen and the mixture refluxed for 5 minutes (with development of a dark brown colour). Methyl iodide (3 g.) was added, the colour being rapidly discharged. Water (20 c.c.) was added, the product taken up in ethyl acetate, and the solvent removed under reduced pressure. A dark red oil was obtained which failed to crystallise and which was hydrolysed by 2 hours' refluxing under nitrogen with sulphuric acid (4 c.c.), water (20 c.c.), and alcohol (15 c.c.), followed by 1 hour's refluxing with sodium hydroxide solution (5%). The dark red neutral oil obtained gave a dark purple 2 : 4-dinitrophenylhydrazone, m. p. 273°, identical with that obtained from the initial ketone; no other pure compound could be isolated.

1 : 2 : 3 : 4-*Tetrahydro*-1-*keto*-6-*methoxynaphthalene*.—Slight modifications of this preparation (Stork, *J. Amer. Chem. Soc.*, 1947, **69**, 576) have been made which somewhat increase the ease of working-up. The oxidation was carried out on tetrahydromethoxynaphthalene (54 g.) as described; the acetic acid solution was then evaporated under reduced pressure to a dark green tar. This became granulated on trituration with ether (total, 1 l.) and was finely ground in a mortar with ethyl acetate (total, 1 l.). The combined extracts were distilled, the product, b. p. 165—170°/18 mm., being collected. It was passed in benzene through a short column of alumina. On concentration of the solvent the colourless tetrahydroketomethoxynaphthalene (36 g.) crystallised; it had m. p. 78°.

1 : 2 : 3 : 4 : 5 : 8-*Hexahydro*-1-*hydroxy*-6-*methoxynaphthalene*.—Sodium (20 g.) in small pieces was added with stirring to a solution of the methoxytetralone (17·6 g.) in ammonia (500 c.c.) and ethanol (200 c.c.). On completion of the reaction, water (500 c.c.) was added, and the mixture extracted with ether. The extract was washed with water, dried (K_2CO_3), and evaporated at room temperature under nitrogen. The oil obtained crystallised overnight in the refrigerator after addition of a little light petroleum (b. p. 40—60°). The 1 : 2 : 3 : 4 : 5 : 8-hexahydro-1-hydroxy-6-methoxynaphthalene (10 g.) was obtained as prisms, m. p. 76—77° after recrystallisation in the refrigerator from light petroleum (b. p. 40—60°) containing a little ether.

1 : 2 : 3 : 4 : 5 : 8-*Hexahydro*-1-*keto*-6-*methoxynaphthalene*.—A solution of the compound above (8 g.) in toluene (35 c.c.) and acetone (20 c.c.) containing aluminium *iso*propoxide (1·5 g.) was refluxed under nitrogen for 4·5 hours. The solution was then decomposed with water (15 c.c.), the aqueous solution extracted with ether (200 c.c.), and the solvent evaporated under reduced pressure in nitrogen. The resulting oil could be distilled almost quantitatively at 130°/1 mm., but could also be crystallised directly in the refrigerator under nitrogen after addition of light petroleum (b. p. 40—60°; 20 c.c.). 1 : 2 : 3 : 4 : 5 : 8-*Hexahydro*-1-*keto*-6-*methoxynaphthalene* was obtained as long colourless needles (6 g.), m. p. 46—48° (Found: C, 73·6; H, 8·2. $C_{11}H_{14}O_2$ requires C, 74·15; H, 7·9%). The ultra-violet absorption maximum was at 238 mμ ($\varepsilon = 9320$) in accord with the assigned structure. 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydro*-1 : 6-*diketonaphthalene dioxime* was obtained by the action of aqueous hydroxylamine hydrochloride at 70°, followed by the addition of sodium acetate, and, crystallised from aqueous ethanol, had m. p. 185° (decomp.) (Found: C, 62·3; H, 7·6; N, 14·3. $C_{10}H_{14}O_4N_2$ requires C, 61·9; H, 7·2; N, 14·4%). Use of a higher proportion (*ca.* 5 g.) of aluminium *iso*propoxide gave a product, b. p. 130°/1·5 mm., which did not crystallise but gave the same dioxime; it probably contained some of the fully conjugated compound.

1 : 2 : 3 : 4 : 8 : 9-*Hexahydro*-1-*keto*-6-*methoxy*-9-*methylnaphthalene*.—The above hexahydroketomethoxynaphthalene (6·0 g.) in ether (30 c.c.) was added to a solution of potassium amide (from the metal, 1·5 g.) in liquid ammonia (100 c.c) with development of a deep yellow-brown colour. After 4 minutes, methyl iodide (15 g.) was added cautiously, the colour being discharged in a rapid reaction. Water (150 c.c.) was then added; the oil obtained by ether-extraction was then distilled (5·7 g.) (b. p. 115°/0·4 mm.). The reactions below show that it was chiefly 1 : 2 : 3 : 4 : 8 : 9-*hexahydro*-1-*keto*-6-*methoxy*-9-*methylnaphthalene* (Found: C, 75·1; H, 8·6. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). The assigned structure was supported by the absorption max. at 274 mμ ($\varepsilon = 5200$), inflexion at 241 mμ ($\varepsilon = 4450$).

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro*-1 : 6-*diketo*-9-*methylnaphthalene*.—The above enol ether (2·5 g.) and 0·5N-hydrochloric acid (10 c.c.) were heated on the steam-bath with shaking for 10 minutes under nitrogen. The product was extracted with ether (4 × 50 c.c.), then dried (Na_2SO_4), and the solvent removed under reduced pressure. The resulting oil could be distilled (b. p. 106—108°/10^{-3} mm.) (Found: C, 73·6; H, 8·2. Calc. for $C_{11}H_{14}O_2$: C, 74·1; H, 7·9%) and had $\lambda_{max.}$ 243—244 ($\varepsilon = 10{,}390$) and 342 mμ ($\varepsilon = 490$) and $\lambda_{min.}$ 327 mμ ($\varepsilon = 460$). Wendler *et al.* (*loc. cit.*) give $\lambda_{max.}$ 244 mμ ($\varepsilon = 12{,}335$) for pure 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-1 : 6-diketo-9-methylnaphthalene. The distilled product crystallised, but it was not necessary to distil it. The crude product was extracted with boiling light petroleum (b. p. 40—60°) until

only a small amount of a yellowish gum (A) was left, and on concentration of the extract and addition of pure ether (6 c.c.) the diketone crystallised as massive prisms on storage in the refrigerator. The mother-liquor was concentrated and added to (A) and the whole passed in ether (3 c.c.) through neutral alumina (40 g.); ether–light petroleum (b. p. 40—60°) (1 : 1) was used as eluent. The first fractions contained more of the crystallisable diketone, and the later fractions a small amount of 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-1-keto-5-methylnaphthalene, crystallising as cream-coloured prisms (from aqueous acetone), m. p. 198—200° undepressed by an authentic specimen. The combined diketone fractions were recrystallised from ether–light petroleum (b. p. 40—60°) (2 : 1), to give the massive prisms of 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-1 : 6-diketo-9-methylnaphthalene (0·95 g.), m. p. 49°, undepressed by an authentic specimen. The infra-red spectrum of the molten substance was also identical with that of the authentic material, having bands at the following wave-lengths (μ) (s = strong; m = medium; w = weak; s-b = side-band): 3·43s 5·84s, 5·99s, 6·17m, 6·84s-b, 6·90s, 7·05s, 7·27s, 7·42s, 7·55s, 7·88s, 8·08s, 8·47s, 8·66s, 9·30m, 9·75s-b, 9·85s, 10·1w, 10·42m, 10·64s, 11·38s, 11·67s, 12·05s, and 12·93m. The band at 5·84 μ doubtless is due to the saturated C·C·CO group, and that at 5·99μ to the αβ-unsaturated carbonyl group. The bis-2 : 4-dinitrophenylhydrazone separated from tetrahydrofuran as a brick-red microcrystalline powder, m. p. 247—248° undepressed by an authentic specimen (Found: C, 51·8; H, 4·3; N, 20·8. Calc. for $C_{22}H_{22}O_8N_8$: C, 51·3: H, 4·1; N, 20·8%). The dioxime was prepared by refluxing the diketone with hydroxylamine acetate in aqueous methanol for 1·5 hours, and crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as colourless needles, m. p. 204°.

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydro*-1-*hydroxy*-6-*keto*-9-*methylnaphthalene*.—The above hexahydroketomethoxymethylnaphthalene (3 g.) in ether (10 c.c.) was reduced in the usual manner with lithium aluminium hydride (1 g.) in ether (20 c.c.). The crude reduction product was heated on the steam-bath for 10 minutes with 0·5N-hydrochloric acid (5 c.c.), then extracted with ether (3 × 20 c.c.), and evaporated. The product was taken up in ether (5 c.c.), water (5 drops) added, and the solution left in the refrigerator overnight. The 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-1-*hydroxy*-6-*keto*-9-*methylnaphthalene monohydrate* (800 mg.) crystallised in elongated colourless prisms, m. p. 59—60° (Found: C, 66·8; H, 9·0. $C_{11}H_{18}O_3$ requires C, 66·7; H, 9·1%). The structure was supported by the absorption max. at 240 mμ (ε = 14,700). When dried in a vacuum the crystals liquefied and the anhydrous substance could not be induced to crystallise. The combined mother-liquors were passed through a column of alumina (30 g.) in ether–light petroleum (b. p. 40—60°) (1 : 2), to give an oil (A) (350 mg.), and further elution gave the above keto-alcohol (60 mg.). The oil (A) was treated with Brady's reagent, and the product crystallised from tetrahydrofuran–ethanol, to give 2 : 3 : 4 : 6 : 7 : 8-*hexahydro*-2-*keto*-1-*methylnaphthalene* 2 : 4-*dinitrophenylhydrazone* as dark purple flat prisms, m. p. 192° (Found: C, 59·55; H, 5·1. $C_{17}H_{18}O_4N_4$ requires C, 59·6; H, 5·3%). The constitution was supported by the absorption max. at 404 mμ, (ε = 62,400) (cf. Braude and Jones, *J.*, 1945, 502).

5 : 6 : 7 : 8-*Tetrahydro*-8-*methylindane*-1 : 5-*dione* (XX).—β-*m*-Methoxyphenylpropionic acid (10 g.) was added to a solution of phosphoric anhydride (25 g.) in phosphoric acid (*d* 1·5; 25 c.c.) at 130°, and the mixture stirred at that temperature for 15 minutes and then cooled. Water (100 c.c.) was added, and the solid taken up in ethyl acetate and washed with 0·5N-sodium hydroxide, dried, and evaporated under reduced pressure. 5-Methoxyindan-1-one crystallised from ethyl acetate as cream-coloured needles (5·8 g.), m. p. 108°.

This product (3 g.) was reduced with sodium (4·6 g.) after addition in ethanol (70 c.c.) to ammonia (150 c.c.). The 4 : 7-*dihydro*-1-*hydroxy*-5-*methoxyindane* could be distilled under nitrogen (b. p. 120°/1 mm.), but was best purified by chromatography in ether–light petroleum (b. p. 40—60°) (1 : 1) on alkaline alumina (30 g.). After neglect of a small oily first fraction, the bulk of the product crystallised in the refrigerator from light petroleum (b. p. 40—60°) as colourless elongated prisms (1·7 g.), m. p. 50° (Found: C, 72·2; H, 8·6. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%). Treatment with Brady's reagent gave the deep red 2 : 4 : 5 : 6-*tetrahydro*-6-*keto*-*indene* 2 : 4-*dinitrophenylhydrazone*, m. p. 178° (Found: C, 57·4; H, 4·45; N, 17·6. $C_{15}H_{14}O_4N_4$ requires C, 57·3; H, 4·45; N, 17·8%). The constitution of this was supported by its absorption max. at 397 mμ (ε = 32,900) and min. at 332 mμ (ε = 7180) in chloroform.

The dihydrohydroxymethoxyindane (3·7 g.) in toluene (35 c.c.) was oxidised under nitrogen with aluminium *iso*propoxide (0·9 g.) and acetone (20 c.c.) in the same manner as the naphthalene derivative above. The product, obtained after addition of water, ether-extraction, and evaporation of the solvent under reduced pressure in nitrogen, could be distilled (b. p. 106°/0·01 mm.), but was best crystallised in the refrigerator under nitrogen after addition of a little light petroleum (b. p. 40—60°). 4 : 7-*Dihydro*-5-*methoxyindan*-1-*one* (2·7 g.) formed colour-

less needles, m. p. 82—83° (Found: C, 73·5; H, 7·4. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%). It was very unstable in air. Hot aqueous hydroxylamine hydrochloride, followed by sodium acetate, gave 5 : 6 : 7 : 8-*tetrahydroindane*-1 : 5-*dione dioxime*, m. p. 190° (decomp.) (Found: C, 60·3; H, 6·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7%).

The dihydroketomethoxyhydrindene (2·7 g.) in ether (10 c.c.) was added to potassium amide (from the metal, 0·75 g.) in ammonia (100 c.c.), followed by methyl iodide to discharge the deep yellow colour. The product (2·9 g.) was worked up as for the naphthalene compound above. The crude substance (1·2 g.) was hydrolysed by 0·5N-hydrochloric acid (1 c.c.) on the steam-bath for 5 minutes. The product was taken up in ether, washed with sodium hydrogen carbonate solution, and dried, and the solvent was evaporated. Extraction with boiling light petroleum (b. p. 40—60°) (3 × 10 c.c.) and evaporation, followed by chromatography in ether–light petroleum (b. p. 40—60°) (2 : 1) on neutral alumina (20 g.), gave a preliminary oily fraction, followed by a crystalline solid and finally a yellow gum (A). 5 : 6 : 7 : 8-Tetrahydro-8-methylindane-1 : 5-dione recrystallised from light petroleum (b. p. 40—60°) as colourless prisms (70 mg.), m. p. 71—72° (Found: C, 73·5; H, 7·2. Calc. for $C_{10}H_{12}O_2$: C, 73·2; H, 7·3%). The ultra-violet absorption showed max. at 236 (ε = 10,200) and 290 mμ (ε = 375) and a min. at 278 mμ (ε = 330) in ethanol; Wieland and Miescher (*loc. cit.*) gave m. p. 71—72° and $\lambda_{max.}$ 235 mμ (ε = 12,000). The residue from the petroleum extractions was added to (A), and the whole dissolved in ether. Fractional extraction with sodium hydroxide solution removed two compounds (as bright yellow solutions) with m. p. 180° and 240° (decomp.) respectively. These are evidently phenolic ketones, and were not further investigated.

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THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 22nd,* 1952.]

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328. *Condensation Products of Phenols and Ketones. Part VIII.* Proof of the Flavan Structure of the Dimerides of* o-iso*Propenylphenol, and of* 3-iso*Propenyl*-o- *and* -p-*cresol.*†

By WILSON BAKER, R. F. CURTIS, and J. F. W. MCOMIE.

The dimeride of 4-*iso*propenyl-*m*-cresol, which was proved in Part VI to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I), has been degraded by oxidation and partial decarboxylation to 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). This acid has also been obtained by the degradation of the dimerides of *o-iso*propenylphenol and of 3-*iso*propenyl-*o*- and -*p*-cresol, proving that these compounds are all 2′-hydroxy-2 : 4 : 4-trimethylflavans.

Reaction of 2 : 4 : 4-trimethylchroman-2-carboxylic acid and homologues with copper chromite–quinoline is abnormal, as decarboxylation does not occur; instead, loss of the elements of carbon monoxide leads to 2-hydroxy-2 : 4 : 4-trimethylchromans, and simultaneous loss of the elements of carbon monoxide and water to 2 : 4 : 4-trimethylchromens. The tendency of 2′-hydroxy-2 : 4 : 4-trimethylflavans to form crystalline complexes (Part VII *) is further illustrated by the examples now given; an exception is provided by the dimeride of 3-*iso*propenyl-*o*-cresol, which is sterically hindered.

m-CRESOL and acetone condense in presence of hydrogen chloride to give a compound $C_{20}H_{24}O_2$, which is also obtained by dimerisation of the intermediate 4-*iso*propenyl-*m*-cresol. A full account of this substance was given in Part VI (Baker, Curtis, and McOmie, *J.*, 1951, 76), where it was proved to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I) by an unambiguous synthesis of the oxidation product 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II). It was desired to extend this investigation to other products obtained

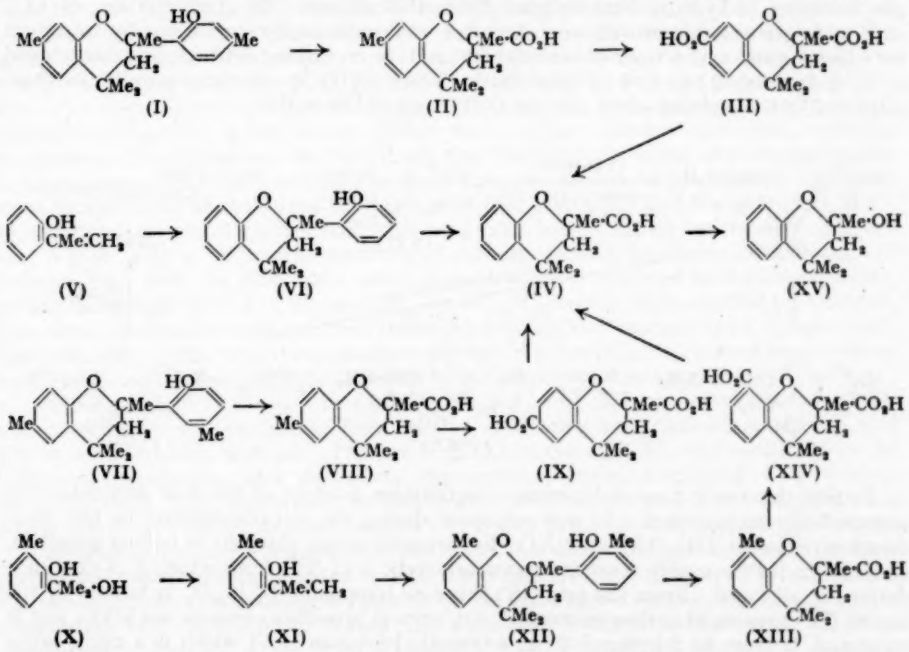
* Part VII, *J.*, 1951, 84.

† The nomenclature of cresols in this paper is based on Me = 1.

either by the direct condensation of acetone with certain phenols, or by the dimerisation of *o-iso*propenylphenols prepared in other ways. The probability that these compounds were all derived from 2′-hydroxy-2 : 4 : 4-trimethylflavan was first advanced by Baker and Besly (*Nature*, 1939, **144**, 865; Part V, *J.*, 1940, 1105), but factual evidence was then only available in the case of the dimeride of 4-*iso*propenyl-*m*-cresol. The suggestion that the dimerides had the same basic structure was made on the grounds that they were prepared by similar methods, that they were all saturated, monohydroxy-phenols possessing extremely weak phenolic functions, and that they reverted to the *o-iso*propenylphenols when distilled at atmospheric pressure. However, to adopt the method of proof employed in Part VI in the case of the dimeride of 4-*iso*propenyl-*m*-cresol would have involved a lengthy total synthesis of a separate substituted 2 : 4 : 4-trimethylchroman-2-carboxylic acid in each case.

The decision was therefore made to attempt the preparation from each of the supposed flavans of a common degradation product which would contain sufficient of the original structure to afford an unambiguous proof of the nature of the flavan. The obvious compound for this purpose was 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV), for the following reasons : (1) the carboxyl group would result from the oxidation of any hydroxyphenyl group in position 2, and a carboxyl group in this position is known to be very resistant towards decarboxylation (Part V, *loc. cit.*); (2) substituent groups of a wide variety of types, including methyl, would be capable of elimination from the benzo-ring, and even very vigorous methods might be used owing to the great stability of acids of the type (IV).

The acid (IV) was first prepared from the *m*-cresol–acetone condensation product (I) of established structure, *via* 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II), the 7-methyl group of which was oxidised by boiling alkaline potassium permanganate to give 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). This acid (III) lost the aromatic

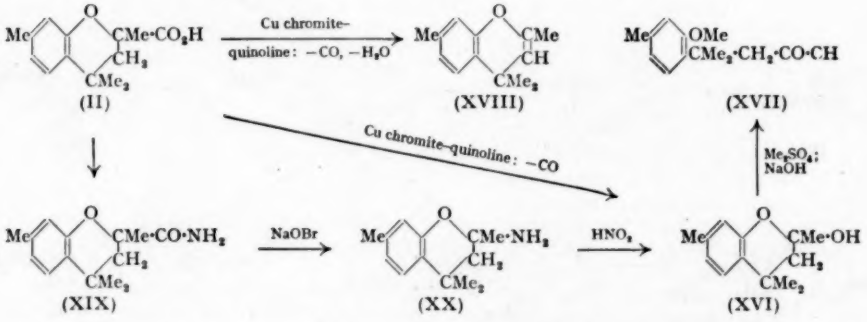


carboxyl group when boiled with copper chromite in quinoline and thus yielded the crystalline reference compound 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV) (for a by-product of this reaction see p. 1776).

*o-iso*Propenylphenol (V) is not formed by the condensation of phenol with acetone under acid conditions, as reaction occurs in the *p*-position to the hydroxyl group, giving 2 : 2′-di-*p*-hydroxyphenylpropane (Dianin, *J. Russ. Phys. Chem. Soc.*, 1891, **23**, 488, 523, 601). It was therefore prepared from the sodium salt of methyl salicylate and methylmagnesium iodide, followed by thermal dehydration of the resulting tertiary carbinol (Fries, Gross-Selbeck, and Wicke, *Annalen*, 1914, **402**, 305). Dimerisation was effected with anhydrous hydrogen chloride, and the crystalline dimeride (characterised as the acetyl derivative and the methyl ether) was then oxidised with potassium permanganate in boiling acetone, giving 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). The dimeride of *o-iso*propenylphenol must therefore be 2′-hydroxy-2 : 4 : 4-trimethylflavan (VI).

With *p*-cresol the proof of structure of the condensation product with acetone followed exactly the steps used in the case of the derivative from *m*-cresol. The condensation product, finally proved to be 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII), was degraded by potassium permanganate in acetone to 2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid (VIII), then further oxidised by boiling alkaline potassium permanganate to 2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid (IX), and finally partially decarboxylated with copper chromite in boiling quinoline to give once again 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV). The formation of the last acid proves the structures assigned to the compounds (VII), (VIII), and (IX).

The final case studied was that of the dimeride (XII) of 3-*iso*propenyl-*o*-cresol (XI). The dimeride (XII) is not obtained by condensation of acetone with *o*-cresol in presence of acid, as attack occurs in the *p*-position to the hydroxyl group, giving either 6 : 6′-dihydroxy-3 : 3 : 5 : 3′ : 3′ : 5′-hexamethylbis-1 : 1′-*spiro*indane, or 2 : 2-di-(4-hydroxy-3-methylphenyl)propane, according to the reaction conditions (see Part IV, Baker and Besly, *J.*, 1939, 1421). 3-*iso*Propenyl-*o*-cresol was obtained from the sodium salt of methyl *o*-cresotate by reaction with methylmagnesium iodide and thermal dehydration of the resulting (2-hydroxy-3-methylphenyl)dimethylcarbinol (X). Dimerisation of (XI) with hydrogen chloride proved very slow, but was conveniently carried out by treatment for a few minutes with a trace of iodine at 60°, and the crystalline dimeride was then proved to be 2′-hydroxy-2 : 4 : 4 : 8 : 3′-pentamethylflavan (XII) by reactions parallel to those employed in the *p*-cresol series, *i.e.*, *via* (XIII) and (XIV) to (IV).



During this work a second common degradation product of the four dimerides was unexpectedly encountered. It was produced during the decarboxylation of the three dicarboxylic acids (III), (IX), and (XIV) by means of copper chromite in boiling quinoline, and also in the same way from the monocarboxylic acid (IV) from which it is doubtless derived in all cases. From the acid (IV) this new compound, $C_{12}H_{16}O_2$, is formed by the loss of the elements of carbon monoxide, and, since it is neither phenolic nor acidic and is saturated, it must be 2-hydroxy-2 : 4 : 4-trimethylchroman (XV) which is a cyclic semiketal. As this compound was not available in quantity, its homologue, obtained similarly from the acid (II) derived from the *m*-cresol–acetone condensation product, was investigated, and was proved by its reactions to be 2-hydroxy-2 : 4 : 4 : 7-tetramethyl-

chroman (XVI). Methylation of (XVI) with methyl sulphate and alkali yielded 4-(2-methoxy-4-methylphenyl)-4-methylpentan-2-one (XVII), a ketone which had been previously synthesised and characterised as its 2 : 4-dinitrophenylhydrazone (Part VI, *loc. cit.*); and, as a semi-ketal, (XVI) reacted with ethanol and hydrogen chloride to give 2-ethoxy-2 : 4 : 4 : 7-tetramethylchroman. The analogous compounds, 2-hydroxy-2 : 4 : 4 : 6- and -2 : 4 : 4 : 8-tetramethylchroman, were obtained under similar reaction conditions from the acids (VIII) and (XIII). The ketone (XVII) undergoes a complex reaction with acetic–hydrobromic acids, giving 4 : 4 : 7 : 4′ : 4′ : 7′-hexamethylbis-2 : 2′-*spiro*chroman (Baker and Besly, *J.*, 1939, 199).

These 2-hydroxy-2 : 4 : 4-trimethylchromans differ widely in their properties from compounds claimed to have the same structures (Niederl, *J. Amer. Chem. Soc.*, 1929, **51**, 2426) which were prepared by the condensation of phenol or a cresol with mesityl oxide in presence of concentrated sulphuric acid. The melting points given by Niederl, except for that of the supposed 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), differ from those which we obtain, and our 2-hydroxy-2 : 4 : 4-trimethylchromans, unlike Niederl's compounds, are stable to acids and alkalis and do not readily undergo dehydration. No proof of structure was advanced by Niederl, and moreover we have not been able to repeat his experiments, from which we have obtained only red tars; failure has also been reported by Smith and Prichard (*ibid.*, 1940, **62**, 771).

The observation that the carboxylic acids (II), (III), (IV), (IX), and (XIV), which resemble tertiary carboxylic acids in that they possess no α-hydrogen atom, lose the elements of carbon monoxide (the actual liberation of carbon monoxide has not been established) and yield 2-hydroxychromans when boiled in quinoline with copper chromite, may be a general reaction for this type of compound. Olefin formation has also been observed when the acids (II) and (XIII) are boiled with copper chromite in quinoline (the necessarily small scale of the reactions precluded the isolation of olefins in the other cases). From the acid (II) the liquid olefin, 2 : 4 : 4 : 7-tetramethylchromen (XVIII), was isolated and characterised as its tribromo-dibromide, and this derivative was also obtained by the action of bromine on 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI). Attempts to dehydrate the hydroxychroman (XVI) to the chromen (XVIII) by boiling it in quinoline either with or without copper chromite were unsuccessful, and it is concluded that these 2-methylchroman-2-carboxylic acids, when boiled with copper chromite–quinoline, undergo simultaneous decompositions to yield both the 2-hydroxychromans and the chromens. In connection with these reactions, tertiary acids are known to lose carbon monoxide when treated with concentrated sulphuric acid [see Bistrzycki and Mauron, *Ber.*, 1907, **40**, 4370 and references there cited; this behaviour is also shown by the acid (II), see Part VI, *loc. cit.*, p. 77], with formation of tertiary alcohols or olefins (Bistrzycki and Reintke, *Ber.*, 1905, **38**, 839), but a much closer analogy is provided by α-methoxy-acids, R·CH(OMe)·CO_2H (R = *n*-C_5H_{11}, *n*-$C_{10}H_{21}$, or *n*-$C_{16}H_{33}$) which, when distilled with copper, give carbon monoxide, methanol, and aldehydes R·CHO (Darzens and Levy, *Compt. rend.*, 1933, **196**, 348). This type of decomposition would be followed in the cases of the chroman-2-carboxylic acids by semi-ketal cyclisation to the 2-hydroxychromans.

Additional proof of the structure of 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) was obtained by its preparation from 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (II) by an alternative method. The amide (XIX) of the acid (II) was submitted to the Hofmann degradation with potassium hypobromite, giving 2-amino-2 : 4 : 4 : 7-tetramethylchroman (XX), and when this was treated with nitrous acid it gave in 10% yield 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) identical with that prepared previously.

Preparation of o-iso*Propenylphenols and their Dimerides.*—The previous work on 4-*iso*propenyl-*m*-cresol and its dimeride was reviewed in Part VI (*loc. cit.*). The occasion of the establishment of the flavan structures of the dimerides mentioned in the title is an appropriate one on which to review the somewhat confused earlier work on these compounds.

o-iso*Propenylphenol* (V) *and its dimeride* (VI). *o-iso*Propenylphenol (V) has been reported to be preparable from: (1) methylmagnesium iodide and methyl salicylate followed by dehydration of the tertiary carbinol (Béhal and Tiffeneau, *Bull. Soc. chim.*,

1908, **3**, 315; details not given); (2) methyl salicylate methoxymethyl ether and methylmagnesium iodide, followed by acid hydrolysis (Hoering and Baum, D.R.-P. 208,886, 208,962; see *Chem. Zentr.*, 1909, I, 1522); (3) 2-hydroxy-β-methylcinnamic acid by the action of heat (Fries and Volk, *Annalen*, 1911, **379**, 95); (4) the sodium salt of methyl salicylate and methylmagnesium iodide (Fries, Gross-Selbeck, and Wicke, *ibid.*, 1914, **402**, 305); (5) phenol, allyl alcohol, and sulphuric acid (Niederl, Smith, and McGreal, *J. Amer. Chem. Soc.*, 1931, **53**, 3391); (6) phenyl *iso*propenyl ether by rearrangement (Niederl and Storch, *ibid.*, 1933, **55**, 284); (7) phenol, allyl chloride, and sulphuric acid (Smith and Niederl, *ibid.*, p. 4151); (8) phenol, allyl alcohol or trimethylene glycol, and phosphoric acid (Tchitchibabin, *Compt. rend.*, 1934, **198**, 1239; *Bull. Soc. chim.*, 1935, **2**, 517). There is considerable doubt whether methods (5)—(8) give *o-iso*propenylphenol; no characterisation of the products was attempted apart from the boiling points.

The dimeride, m. p. 97°, of *o-iso*propenylphenol was first prepared by reaction of the monomer with hydrogen chloride in ether (Fries, Gross-Selbeck, and Wicke, *loc. cit.*). It was probably also obtained by Smith and Prichard (*J. Amer. Chem. Soc.*, 1940, **62**, 777) as a product, m. p. 95—96°, from the action of hydrogen chloride on *o*-hydroxyphenyldimethylcarbinol in benzene; no opinion was expressed as to its structure. It has also been prepared from methylmagnesium iodide and *cis*-disalicylide (Baker, Ollis, and Zealley, *J.*, 1951, 201). Polymers of *o-iso*propenylphenol were reported to occur in the residue from the destructive distillation of 2:2-di-*p*-hydroxyphenylpropane prepared by condensation of acetone with phenol in presence of acids (von Braun, Anton, Haensel, and Werner, *Annalen*, 1929, **472**, 65). The ultra-violet absorption spectra measurements by Grumez (*Ann. Chim. Phys.*, 1938, **10**, 378, 388) require reinterpretation in terms of the flavan structure (VI) now established.

3-iso*Propenyl*-p-*cresol and its dimeride* (VII). 3-*iso*Propenyl-*p*-cresol has been prepared by the action of heat on β-(2-hydroxy-5-methylphenyl)-β-methylacrylic acid (Fries and Fickewirth, *Ber.*, 1908, **41**, 372; Fries and Volk, *Annalen*, 1911, **379**, 95). Guillaumin (*Bull. Soc. chim.*, 1910, **7**, 379) reported its preparation from methyl *p*-cresotate and methylmagnesium iodide, followed by dehydration of the tertiary alcohol with acetic anhydride and alkaline hydrolysis of the resulting *O*-acetyl derivative of the *iso*propenyl compound; Fries and Volk (*loc. cit.*) were, however, unable to confirm this work. The preparation of 3-*iso*propenyl-*p*-cresol from *p*-cresol, allyl alcohol, or allyl chloride, and sulphuric acid, and by rearrangement of *iso*propenyl *p*-tolyl ether, has been reported by Neiderl *et al.* (*loc. cit.*), but proof of their claims is lacking.

The dimeride (VII), formed from the monomer either on storage alone or by heating it with aqueous hydrochloric acid, is a resin, which distils unchanged *in vacuo*, but reverts to the monomer when distilled at atmospheric pressure (Fries and Fickewirth, *loc. cit.*); it possesses very weak phenolic properties (Fries, Gross-Selbeck, and Wicke, *loc. cit.*). Fries and Fickewirth (*Annalen*, 1908, **362**, 46) also obtained the dimeride from 4:6-dimethylcoumarin by reduction with zinc dust and alkali, followed by dehydration and dimerisation with acid.

Direct production of the dimeride from *p*-cresol, acetone, and hydrogen chloride is described in patents [Schering-Kahlbaum A.-G., B.P. 273,684, 279,856 (1927); F.P. 636,119 (1927); Swiss P. 127,522 (1927); U.S.P. 1,696,769 (1927)]; a crystalline *O*-acetyl derivative was obtained. The preparation now recorded, based on that given by Baker, Curtis, and McOmie (Part VI, *loc. cit.*) for the production of the *m*-cresol analogue, gives the pure compound in 25% yield; its isolation is greatly facilitated by the new observation that the non-crystalline dimeride very readily forms a well-crystallised adduct with one mol. of dioxan. Crystalline adducts with other solvents are mentioned on pp. 1781 and 1785. This dimeride–dioxan adduct loses some dioxan on exposure to the air and gives a powder, but this does not induce crystallisation of a solution of the free dimeride in light petroleum (contrast the behaviour of the related diethyl ether adduct of the dimeride of 4-*iso*propenyl-*m*-cresol; Part VI, *loc. cit.*). The pure dioxan adduct loses all solvent at 100° *in vacuo*, giving a resin which has failed to crystallise; the physical properties of this free dimeride, as are those of the *m*-cresol analogue, are being investigated at the Butterwick Research Laboratories of Imperial Chemical Industries Limited,

Welwyn. The previously described chemical properties of the dimeride (VII) have been confirmed.

In an attempt to improve the yield of 2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid (VIII) by oxidation of the dimeride (VII), an amino-group was introduced into position 3′ in the hope that this *o*-aminophenol would be easily oxidised. Nitration of the acetyl derivative of (VII), followed by hydrolysis, gave 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan which showed the properties of an *o*-nitrophenol, and gave well-crystalline adducts with ethyl ether, methanol, and diethylamine. Reduction with tin and hydrochloric acid led to a very stable stannichloride, but reaction with hydrogen and Raney nickel gave 3′-amino-2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan, characterised as its *N*-acetyl derivative. This amino-compound gave crystalline adducts with methanol and diethylamine. Oxidation with potassium permanganate in acetone gave only yellow quinonoid material.

3-iso*Propenyl-o-cresol* (XI) *and its dimeride* (XII). 3-*iso*Propenyl-*o*-cresol (XI) was prepared by Béhal and Tiffeneau (*Bull. Soc. chim.*, 1910, **7**, 330) by the method used for *o-iso*propenylphenol (V) (above). Guillaumin (*loc. cit.*) described the preparation of (XI) from methyl *o*-cresotate by the process claimed to yield 3-*iso*propenyl-*p*-cresol (above), but doubts have been expressed as to the validity of this work (Fries and Volk, *loc. cit.*). The preparation of (XI) by several methods is reported by Niederl *et al.* (*loc. cit.*), but as with the similar claims to have prepared (V) and 3-*iso*propenyl-*p*-cresol, adequate evidence of success is lacking.

The monomer (XI) and the dimeride (XII) were obtained as described above; the latter has not previously been prepared. The dimeride yielded an *O*-acetyl derivative, but possessed only very weak phenolic properties.

Crystal Complexes formed by 2′-Hydroxy-2 : 4 : 4-trimethylflavans.—The property of forming crystalline adducts with many solvents is characteristic of these compounds. Those formed by 2-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I) were described by Baker, Curtis, and Edwards (Part VII, *loc. cit.*). Crystal complexes given by 2′-hydroxy-2 : 4 : 4-trimethylflavan (VI) and by 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII) are given on pp. 1781 and 1785.

2′-Hydroxy-2 : 4 : 4 : 8 : 3′-pentamethylflavan (XII) has failed to give any such adducts, and this is attributed mainly to the steric effect of the methyl group in position 8. Since all the solvents with which complexes are formed are proton acceptors (bases, ethers, and ketones, although the last two are very weak acceptors), salt formation involving the 2′-hydroxyl group may play a part in the formation of the adducts; hydrogen bonding between the two oxygen atoms may also be involved. It is probable that the solvent molecules in the crystal have their functional groups close to the two oxygen atoms of the 2′-hydroxyflavan, and scale models show that in this case a methyl group in position 8 would exert a considerable, if not a prohibitive, effect against the formation of such complexes. Support for this general structure is derived from the fact that the adducts (over 40 are now known) containing monofunctional molecules are all of the 1 : 1 type, whilst the difunctional molecules dioxan and morpholine give more than usually stable adducts with a flavan : solvent ratio of 2 : 1 in the cases of flavans (I) and (VI), although the adducts from (I) contain, in addition, two molecules of water. However, adducts given by the flavan (VII) with dioxan or morpholine have the 1 : 1 ratio of the components.

Experimental

M. p.s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

2 : 4 : 4-*Trimethylchroman*-2 : 7-*dicarboxylic Acid* (III).—2 : 4 : 4 : 7-Tetramethylchroman-2-carboxylic acid (II) (2·0 g.; Part VI, p. 80) in 5% aqueous sodium carbonate (100 c.c.) was boiled, and potassium permanganate (*ca.* 10 g.) added during 15 minutes. Boiling was continued for 20 minutes, sulphur dioxide passed in, and the solid collected at 0°, washed, and dried (yield 1·96 g.; m. p. 248—250°). Two recrystallisations from light petroleum (b. p. 60—80°)–ethyl acetate gave 2 : 4 : 4-*trimethylchroman*-2 : 7-*dicarboxylic acid* (III) as fine, colourless

needles (1·7 g.), m. p. 261° (Found: C, 63·6; H, 6·1%; equiv., 133. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%; equiv., 132).

Reaction of 2 : 4 : 4-*Trimethylchroman*-2 : 7-*dicarboxylic Acid* (III) *with Copper Chromite–Quinoline.* 2 : 4 : 4-*Trimethylchroman*-2-*carboxylic Acid* (IV) *and* 2-*Hydroxy*-2 : 4 : 4-*Trimethylchroman* (XV).—The acid (III) could not be decarboxylated by (1) soda–lime at 370°, (2) potassium hydroxide at 260° or 300°, (3) heating it with copper chromite in dimethyl- or diethyl-aniline. Success was achieved as below, but the time of heating is critical.

The acid (III) (200 mg.), freshly distilled quinoline (4 c.c.), and copper chromite (400 mg.) were placed in a metal-bath at 260° and boiled for 20 minutes; liberated water caused vigorous bumping. The cooled mixture was poured into concentrated hydrochloric acid (15 c.c.), digested on the water-bath for 15 minutes, diluted with water (20 c.c.), and filtered through sand. The residue was washed with ether (30 c.c.), and the ether combined with the filtrate, shaken, and separated. The aqueous layer was extracted with ether (10 c.c.), and the combined organic extracts were then shaken with saturated sodium hydrogen carbonate which, on acidification, yielded colourless acidic material (47 mg.; m. p. 162—164°). Sublimation at 170°/360 mm. gave colourless needles (29 mg.), m. p. 167—168°, and recrystallisation from benzene–light petroleum (b. p. 60—80°) (1 c.c.) gave 2 : 4 : 4-*trimethylchroman*-2-*carboxylic acid* (IV) as thin rhombs, m. p. 172° (Found: C, 71·0; H, 7·3%; equiv., 216. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%; equiv., 220). The residue from the sublimation (15 mg.; m. p. 258°) had m. p. 258—261° on admixture with a specimen of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III), m. p. 261°.

The ethereal layer containing neutral material yielded a yellow oil which solidified, and crystallised from light petroleum (b. p. 40—60°) in stout prisms, m. p. 90° (28 mg.). A further crystallisation raised the m. p. of this 2-*hydroxy*-2 : 4 : 4-*trimethylchroman* (XV) to 91° (Found: C, 75·3; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%).

o-iso*Propenylphenol* (V) *and* 2′-*Hydroxy*-2 : 4 : 4-*trimethylflavan* (VI).—This compound was prepared as described by Fries, Gross-Selbeck, and Wicke (*Annalen*, 1914, **402**, 305), the intermediate *o*-hydroxyphenyldimethylcarbinol being conveniently dehydrated by heating it in an oil-bath at 180°/560 mm. for ½ hour. The residue was distilled twice through a column, giving *o-iso*propenylphenol (V) as an oil, b. p. 39°/0·4 mm. (Found: C, 80·2; H, 7·3. Calc. for $C_9H_{10}O$: C, 80·6; H, 7·5%). The flavan (VI) was prepared from *o-iso*propenylphenol (V) (30·2 g.) by treatment with a little anhydrous hydrogen chloride while being cooled in water. An exothermic reaction occurred and after 20 minutes the product had become resinous; crystallisation occurred after it had been kept at 40° for 12 hours. The solution in ether (60 c.c.), after extraction with 2N-sodium hydroxide (2 × 30 c.c.), left a viscous oil which gave the flavan (VI) by crystallisation from light petroleum (30 c.c.; b. p. 60—80°) as thin prisms (26·7 g.) (dimorphic, also separates as rhombs), m. p. 97° (Found: C, 80·8; H, 7·5. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%). This compound was characterised as the acetyl derivative, which separated from light petroleum (b. p. 60—80°) in hexagonal prisms, m. p. 97° (Found: C, 77·4; H, 7·1. Calc. for $C_{20}H_{22}O_3$: C, 77·4; H, 7·1%).

2′-*Methoxy*-2 : 4 : 4-*trimethylflavan.*—The flavan (VI) (0·5 g.) and methyl iodide (2 c.c.) were added to a solution of sodium (0·1 g.) in dry methanol (10 c.c.), and the mixture boiled for 2 hours. Excess of methyl iodide and methanol was distilled off, and the residue diluted with water, giving an oil which solidified. Two recrystallisations from aqueous methanol gave the methyl ether as fine prisms (0·275 g.), m. p. 116—117° (Found: C, 80·8; H, 7·7. Calc. for $C_{19}H_{22}O_2$: C, 80·8; H, 7·8%).

2 : 4 : 4-*Trimethylchroman*-2-*carboxylic Acid* (IV).—2′-Hydroxy-2 : 4 : 4-trimethylflavan (VI) (3 g.) in acetone (30 c.c.) was oxidised by rapid addition of a solution of potassium permanganate in acetone (900 c.c.; saturated at the b. p.). The mixture boiled spontaneously and reduction of the permanganate was complete in 1 minute. The acetone was then distilled from the reaction mixture and the residue was shaken with water (100 c.c.), sodium pyrosulphite (metabisulphite) (*ca.* 40 g.), and 2N-hydrochloric acid (40 c.c.), and sulphur dioxide was passed in until the solution was colourless. Two similar oxidations were carried out, and the united products extracted with ether (300 c.c., then 100 c.c.). The ethereal solution was washed with water and shaken 4 times with saturated sodium hydrogen carbonate solution, and the alkaline layer washed with ether and then acidified with hydrochloric acid, giving a pale yellow solid, which was collected at 0° and dried (yield 4·3 g.). Two recrystallisations from benzene (15 c.c.) gave the acid (IV) as rhombs (2·6 g., 35%), m. p. 171—172° alone or mixed with the specimen previously prepared. The identity of the two specimens was also confirmed by *X*-ray powder photographs kindly taken by Dr. T. H. Beavan of this Department.

2'-Hydroxy-2 : 4 : 4 : 6 : 5'-pentamethylflavan (VII).—*p*-Cresol (324 g.) in acetone (116 g.) was saturated with hydrogen chloride at 0°, and the mixture was left in the ice-bath and slowly allowed to reach room temperature. After 2 days the dark product was stirred into 2N-aqueous sodium hydroxide (1 l.), and then became colourless. Dioxan (200 g.) was added, the mixture stirred on the water-bath for 20 minutes and left overnight at 0°, and the solid collected dried over phosphoric anhydride *in vacuo*, and recrystallised from light petroleum (300 c.c.; b. p. 60—80°) with the addition of dioxan (5 c.c.), giving the pure *flavan–dioxan* complex (145 g., 25%) as minute rhombs, m. p. (dissociation, rapid heating) 88—90° (Found : C, 75·3; H, 8·3. $C_{20}H_{24}O_2,C_4H_8O_2$ requires C, 75·0; H, 8·3%).

2'-Hydroxy-2 : 4 : 4 : 6 : 5'-pentamethylflavan (VII), obtained from the dioxan complex by heating it *in vacuo* at 100°, is a colourless resin, b. p. 168°/0·5 mm. without decomposition (Found : C, 80·8; H, 8·2. Calc. for $C_{20}H_{24}O_2$: C, 81·1; H, 8·1%). The phenolic function is very weak; the substance dissolves slightly in aqueous-alcoholic, but not in aqueous, sodium hydroxide, and does not give a ferric chloride reaction. When diethylamine is added to a solution of (VII) in light petroleum the *flavan–diethylamine* complex separates in short, thick needles, m. p. (dissociation) 86—88° [Found : C, 78·1; H, 9·1; N, 3·7; $NH(C_2H_5)_2$ (by loss in weight at 100°), 19·5. $C_{20}H_{24}O_2,NH(C_2H_5)_2$ requires C, 78·1; H, 9·5; N, 3·8; $NH(C_2H_5)_2$, 19·8%]. 2'-Acetoxy-2 : 4 : 4 : 6 : 5'-pentamethylflavan was prepared from the hydroxyflavan (VII) by boiling it with excess of acetic anhydride and sodium acetate for 4 hours. It separated from ethanol in stout needles, m. p. 151° (Found : C, 78·3; H, 7·6. Calc. for $C_{22}H_{26}O_3$: C, 78·1; H, 7·7%). Hydrolysis with alcoholic potassium hydroxide regenerated the hydroxyflavan (VII).

Oxidation of 2'-Hydroxy-2 : 4 : 4 : 6 : 5'-pentamethylflavan (VII). *2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid* (IX) *and 2 : 4 : 4 : 6-Tetramethylchroman-2-carboxylic Acid* (VIII).—The flavan (VII) was oxidised in 3 portions of 3 g. each as described for the flavan (VI). The acidic products were obtained as a pale yellow, slightly resinous material (2·3 g.) which was dissolved in ethylene dichloride (50 c.c.; charcoal), the solution filtered, distilled to a small bulk (5 c.c.), and cooled to 0°, and the solvent decanted from the crystals which separated. This solid was washed with ice-cold light petroleum (b. p. 60—80°) containing a trace of ethanol and dissolved in benzene (25 c.c.), and light petroleum (5 c.c.) was added, whereupon a sparingly soluble acid separated, m. p. 261°. Recrystallisation of this from ethyl acetate–light petroleum (20 c.c.) gave *2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid* (IX) as microcrystalline rhombs (0·22 g.), m. p. 266° (Found : C, 63·7; H, 6·1%; equiv., 133. $C_{14}H_{14}O_5$ requires C, 63·6; H, 6·1%; equiv., 132).

The mother-liquors after removal of the dicarboxylic acid were concentrated (to 2 c.c.), ethylene dichloride (1 c.c.) added, and the dark brown, sticky mass kept overnight at 0°, crystalline material being deposited. This was collected, washed with a few drops of ice-cold ethylene dichloride, and recrystallised from benzene (3 c.c.), giving needles, m. p. 138°. Recrystallisation from aqueous methanol gave *2 : 4 : 4 : 6-tetramethylchroman-2-carboxylic acid* (VIII) as clusters of fine needles (0·23 g.), m. p. 143° (Found : C, 71·9; H, 7·7%; equiv., 238. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%; equiv., 234).

Oxidation of 2 : 4 : 4 : 6-Tetramethylchroman-2-carboxylic Acid (VIII). *2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid* (IX).—The acid (VIII) (0·05 g.) in a solution of sodium carbonate (1 g.) in water (10 c.c.) was boiled, and powdered potassium permanganate slowly added until present in excess for 15 minutes. The solution was cooled, excess of sulphur dioxide passed in, and the precipitated acid collected, washed, and dried (0·049 g.; m. p. 264°). Recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave microcrystalline rhombs, m. p. 266°, showing no depression on admixture with the specimen of 2 : 4 : 4-trimethylchroman-2 : 6-dicarboxylic acid (IX) isolated from the oxidation described above.

Reaction of 2 : 4 : 4-Trimethylchroman-2 : 6-dicarboxylic Acid (IX) *with Copper Chromite–Quinoline. 2 : 4 : 4-Trimethylchroman-2-carboxylic Acid* (IV) *and 2-Hydroxy-2 : 4 : 4-trimethylchroman* (XV).—The acid (IX) (0·200 g.), freshly distilled quinoline (4 c.c.), and copper chromite (0·400 g.) were heated under reflux (metal-bath at 260°) for 20 minutes. The product was then worked up as described for the partial decarboxylation of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). The acidic product (0·055 g.), m. p. 158—160°, was sublimed (160°/360 mm.), giving colourless needles (0·029 g., 20%), m. p. 162—164°. Two recrystallisations from benzene–light petroleum (b. p. 60—80°) (1 c.c.) gave a product, m. p. 172°, alone or mixed with a previous specimen of 2 : 4 : 4-trimethylchroman-2-carboxylic acid (IV), m. p. 172°. The residue from the sublimation (0·022 g.), m. p. 262°, was the unchanged acid (IX). The neutral fraction yielded pale yellow prisms (0·006 g.), m. p. 86—87°, which sublimed

(120°/10 mm.) in needles, m. p. 90°, undepressed when mixed with the previous specimens of 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), m. p. 91°.

Reaction of 2 : 4 : 4 : 6-*Tetramethylchroman-2-carboxylic Acid* (VIII) *with Copper Chromite–Quinoline.* 2-*Hydroxy*-2 : 4 : 4 : 6-*tetramethylchroman.*—The acid (VIII) (0·20 g.), copper chromite (0·2 g.), and quinoline (4 c.c.) were boiled under reflux for 6 hours. The product was worked up as before, giving unchanged acid (0·059 g.), m. p. 142—143°. The ethereal layer gave neutral material, which was crystallised from light petroleum (2 c.c.; b. p. 60—80°) (charcoal). 2-*Hydroxy*-2 : 4 : 4 : 6-*tetramethylchroman* separated as thin rhombs (0·010 g.), which after rapid sublimation (115°/13 mm.) had m. p. 100° (Found: C, 75·7; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

2′-*Acetoxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan.*—2′-Acetoxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (above) (20 g.) in glacial acetic acid (200 c.c.) at 50° was treated dropwise (cooling and vigorous stirring) with concentrated nitric acid (20 c.c.; *d* 1·41) during 2 hours. The deep red solution was poured into water, and the solid collected and recrystallised from ethanol, giving the *nitro*-compound as thick, pale yellow plates (18·5 g.), m. p. 136—137° (Found: C, 68·5; H, 6·5; N, 3·6. $C_{22}H_{25}O_5N$ requires C, 68·9; H, 6·3; N, 3·7%).

2′-*Hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan.*—The preceding acetoxy-compound (16 g.) was stirred with ethanol (160 c.c.) and 2N-sodium hydroxide (40 c.c.) for 2 hours at 40°. Acidification of the deep orange solution gave a yellow solid which was crystallised twice from aqueous methanol, giving the *methanol* complex of 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan as thin, yellow prisms (15·3 g.), m. p. 88—89° (dissociation with loss of methanol) (Found: C, 67·4; H, 7·3; N, 4·0. $C_{20}H_{23}O_4N,CH_4O$ requires C, 67·6; H, 7·2; N, 3·8%). Crystallisation from light petroleum (b. p. 80—100°) gave very pale yellow prisms of the free 2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethyl*-3′-*nitroflavan*, m. p. 100—101° (Found: C, 70·1; H, 6·4; N, 4·4. $C_{20}H_{23}O_4N$ requires C, 70·4; H, 6·7; N, 4·1%). When crystallised from ether, the *diethyl ether* complex separated as pale yellow rhombs, m. p. (rapid heating with loss of ether) 73—74° (Found: C, 69·4; H, 8·0; N, 3·0; $C_4H_{10}O$, by loss of weight at 100°, 17·8. $C_{20}H_{23}O_4N,C_4H_{10}O$ requires C, 69·4; H, 7·95; N, 3·4; $C_4H_{10}O$, 17·8%). From light petroleum containing diethylamine the substance crystallised as the *diethylamine* complex, large, pale yellow rhombs, m. p. (rapid heating with loss of $NHEt_2$) 116—117° (Found: C, 69·6; H, 8·2; N, 6·8; $C_4H_{11}N$, by loss of weight at 120°, 17·7. $C_{20}H_{23}O_4N,C_4H_{11}N$ requires C, 69·6; H, 8·2; N, 6·8; $C_4H_{11}N$, 17·6%).

2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethyl-3′-nitroflavan gives a reddish-orange solution in alcoholic potassium hydroxide, and when boiled with acetic anhydride and anhydrous sodium acetate regenerated the acetyl derivative, m. p. and mixed m. p. 136—137°.

3′-*Amino*-2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethylflavan.*—The methanol complex of the preceding nitro-compound (10·2 g.) in methanol (150 c.c.) was hydrogenated (5 atm.) with a Raney nickel catalyst (*ca.* 10 g.) for 6 hours. The filtrate (Filtercel used) was concentrated (to 50 c.c.) and diluted with water. 3′-*Amino*-2′-*hydroxy*-2 : 4 : 4 : 6 : 5′-*pentamethylflavan* separated from methanol with methanol of crystallisation in microcrystalline rhombs (9·0 g.; m. p. 126—127° with loss of methanol), which after recrystallisation from the same solvent had m. p. 130—131° (Found: C, 73·2; H, 8·2; N, 4·2. $C_{20}H_{25}O_2N,CH_4O$ requires C, 73·5; H, 8·45; N, 4·1%). Removal of the methanol under diminished pressure gave a resin which when dissolved in light petroleum (b. p. 40—60°) containing diethylamine deposited the *diethylamine* complex, m. p. (with loss of $NHEt_2$) 109—110° (Found: C, 74·7; H, 9·0; N, 7·3. $C_{20}H_{25}O_2N,C_4H_{11}N$ requires C, 75·0; H, 9·4; N, 7·3%). The amine gave under normal conditions a diazonium salt which coupled with alkaline β-naphthol. The N-*acetyl* derivative, prepared from the amine (0·200 g.) and acetic anhydride (5 c.c.) at 60° for 10 minutes, followed by addition of water (yield 0·194 g.), separated from ethanol (charcoal) in rhombs, m. p. 214° (Found: C, 74·7; H, 7·6; N, 3·8. $C_{22}H_{27}O_3N$ requires C, 74·8; H, 7·65; N, 4·0%).

(2-*Hydroxy*-3-*methylphenyl*)*dimethylcarbinol* (X).—The preparation of the sodium salt of methyl *o*-cresotate from the ester (84 g.), and sodium (11·5 g.) in toluene (150 c.c.), its reaction with methylmagnesium iodide, and the isolation of the product was carried out as for the preparation of *o-iso*propenylphenol (p. 1780). After saturation of the alkaline solution with carbon dioxide the solid was collected, washed, dried (P_4O_{10}), and crystallised from light petroleum (300 c.c.; b. p. 60—80°) (charcoal) at 0°. (2-Hydroxy-3-methylphenyl)dimethylcarbinol (X) separated as long (*ca.* 3 cm.) needles (63·0 g., 75%), m. p. 77° (Found: C, 72·5; H, 8·6. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·4%).

3-iso*Propenyl*-o-*cresol* (XI).—(2-Hydroxy-3-methylphenyl)dimethylcarbinol (5 g.) was heated for 20 minutes in an oil-bath at 200°/460 mm. Water was rapidly lost and the 3-*iso*-

propenyl-*o*-cresol distilled at 54°/0·5 mm. (Found: C, 81·4; H, 8·4. Calc. for $C_{10}H_{12}O$: C, 81·1; H, 8·1%) (yield 3·6 g.; 81%). Iodine may not be used as a catalyst in this reaction as it causes immediate dimerisation of the *iso*propenyl compound (see below).

2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan (XII).—*3-iso*Propenyl-*o*-cresol (XI) undergoes dimerisation to the flavan (XII) in 72% yield when saturated with hydrogen chloride and kept at 40° for 5 days. The dimerisation is, however, much more rapidly caused by iodine. *3-iso*-Propenyl-*o*-cresol (3·1 g.) was treated at 60° with iodine (8 mg.); a strongly exothermic reaction occurred and the oil became very viscous within 5 minutes. After 15 minutes the product was dissolved in ether (20 c.c.), washed with aqueous sodium sulphite, then with water, and dried, and the ether distilled, leaving a pale yellow resin which was crystallised from light petroleum (10 c.c.; b. p. 40—60°) at 0°. *2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan* (XII) separated as stout prisms (2·4 g.), m. p. 70—71° (Found: C, 80·7; H, 8·2. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%). The flavan distils unchanged at 162—163°/0·5 mm., and, like the other flavans of the series, it shows only very weak phenolic properties and gives no ferric chloride reaction. The *acetyl* derivative crystallised from aqueous methanol in prisms, m. p. 103° (Found: C, 78·4; H, 7·8. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%).

Oxidation of 2'-Hydroxy-2 : 4 : 4 : 8 : 3'-pentamethylflavan (XII). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid* (XIV) *and 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid* (XIII).—The flavan (XII) was oxidised in 3 portions of 3 g. each as described above for the oxidation of 2'-hydroxy-2 : 4 : 4-trimethylflavan (VI), and the acidic products (2·2 g.) were isolated in the same way. Fractional crystallisation from benzene (7 c.c.) gave the less soluble *2 : 4 : 4-trimethylchroman-2 : 8-dicarboxylic acid* (XIV), which was finally crystallised from ethyl acetate–light petroleum (b. p. 60—80°), giving microcrystalline rhombs (0·028 g.), m. p. 198°, undepressed on admixture with the specimen prepared as described below. Concentration of the mother-liquors gave *2 : 4 : 4 : 8-tetramethylchroman-2-carboxylic acid* (XIII) as clusters of thin needles (1·2 g., 25%), m. p. 143—144°, which after recrystallisation from benzene–light petroleum (b. p. 60—80°) had m. p. 151° (Found: C, 71·9; H, 7·7%; equiv., 238. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%; equiv., 234).

Oxidation of 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid (XIII). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid* (XIV).—The acid (XIII) (1·0 g.) in sodium carbonate (2·5 g.) and water (50 c.c.) was boiled under reflux and powdered potassium permanganate (*ca.* 5 g.) added during 15 minutes. Boiling was continued for 20 minutes, sulphur dioxide passed in until the solution was colourless, and the precipitated acidic material collected and crystallised twice from ethyl acetate–light petroleum (b. p. 60—80°). *2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic acid* (XIV) separated as rhombs (0·87 g.), m. p. 198° (Found: C, 63·3; H, 6·0%; equiv., 127. $C_{14}H_{16}O_6$ requires C, 63·6; H, 6·1%; equiv., 132).

Reaction of 2 : 4 : 4-Trimethylchroman-2 : 8-dicarboxylic Acid (XIV) *with Copper Chromite–Quinoline. 2 : 4 : 4-Trimethylchroman-2-carboxylic Acid* (IV) *and 2-Hydroxy-2 : 4 : 4-trimethylchroman* (XV).—The dicarboxylic acid (XIV) (0·200 g.) was boiled with quinoline and copper chromite and the products were isolated as described for the partial decarboxylation of 2 : 4 : 4-trimethylchroman-2 : 7-dicarboxylic acid (III). The acidic material, m. p. 170—171° (0·071 g.), was recrystallised from benzene–light petroleum (b. p. 60—80°) (1 c.c.), giving rhombs, m. p. 172° alone or mixed with a specimen of 2 : 4 : 4-trimethylchroman-2-carboxylic acid, m. p. 172°.

The neutral ethereal extract yielded a yellow oil which separated from light petroleum (1 c.c.; b. p. 60—80°) in pale yellow prisms (0·012 g.), m. p. 88—89°; recrystallisation gave 2-hydroxy-2 : 4 : 4-trimethylchroman (XV), m. p. 91°, alone or mixed with the material, m. p. 91°, previously prepared.

Reaction of 2 : 4 : 4 : 8-Tetramethylchroman-2-carboxylic Acid (XIII) *with Copper Chromite–Quinoline. 2-Hydroxy-2 : 4 : 4 : 8-tetramethylchroman and 2 : 4 : 4 : 8-Tetramethylchromen.*—The acid (XIII) (2·8 g.), copper chromite (1·4 g.), and quinoline (10 c.c.) were boiled under reflux in a rotating flask for 2 hours. The product was worked up as previously described, giving unchanged acid (1·10 g.), m. p. 150°, and a neutral oil which partly crystallised. The solid was separated and washed with light petroleum (b. p. 40—60°), giving *2-hydroxy-2 : 4 : 4 : 8-tetramethylchroman* as hexagonal prisms (0·104 g.), m. p. 60°. Two further crystallisations from light petroleum raised the m. p. to 62—63° (Found: C, 75·5; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

The non-crystalline material from the separation was distilled, giving *2 : 4 : 4 : 8-tetramethylchromen* as a liquid (0·046 g.), b. p. 56—58°/0·3 mm. (Found: C, 83·1; H, 8·5. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%), and a residue from which a further quantity of 2-hydroxy-2 : 4 : 4 : 8-tetramethylchroman (0·044 g.) was obtained.

Reaction of 2 : 4 : 4-*Trimethylchroman-2-carboxylic Acid* (IV) *with Copper Chromite–Quinoline.* 2-*Hydroxy*-2 : 4 : 4-*trimethylchroman* (XV).—The acid (IV) (0·500 g.), quinoline (5 c.c.), and copper chromite (0·5 g.) were boiled (metal-bath at 260°) for 4 hours, and the products isolated as previously described. The acidic fraction yielded unchanged acid (IV) (0·081 g.), m. p. and mixed m. p. 172°. The neutral fraction was distilled, giving a greenish-yellow oil which crystallised from light petroleum (1 c.c.; b. p. 60—80°) in thin prisms, m. p. 87—89° (0·062 g.). Recrystallisation from light petroleum (b. p. 40—60°) gave 2-hydroxy-2 : 4 : 4-trimethylchroman (XV) as prisms, m. p. 91°, either alone or mixed with the specimens previously prepared.

Reaction of 4-(2-*Methoxy*-4-*methylphenyl*)-4-*methylpentan*-2-*one* (XVII) *with Hydrobromic and Acetic Acids.*—The ketone (XVII) (2·0 g.), hydrobromic acid (5 c.c.; *d* 1·48), and acetic acid (15 c.c.) were boiled for 6 hours, poured into water, and extracted with ether, and the extract was shaken with 2N-sodium hydroxide, which on acidification yielded a trace of phenolic material. The ethereal layer was distilled, giving a resin which crystallised from aqueous methanol. 4 : 4 : 7 : 4′ : 4′ : 7′-Hexamethylbis-2 : 2′-*spiro*chroman separated as hexagonal plates (0·409 g.), m. p. and mixed m. p. with an authentic specimen (see Baker and Besly, *J.*, 1939, 199) 132° (Found: C, 82·2; H, 8·3. Calc. for $C_{22}H_{28}O_2$: C, 82·2; H, 8·3%).

Reaction of 2 : 4 : 4 : 7-*Tetramethylchroman-2-carboxylic Acid* (II) *with Copper Chromite–Quinoline.* 2-*Hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI) *and* 2 : 4 : 4 : 7-*Tetramethylchromen* (XVIII).—The statement (Part V, p. 1105) that 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid is not decarboxylated in boiling quinoline in presence of copper chromite is correct, but the reaction was not then continued long enough to enable the hydroxy-compound (XVI) to be isolated. The acid (II) (2·0 g.) and copper chromite (1·0 g.) were boiled in quinoline (8 c.c.) for 6 hours. The product was worked up as described in earlier reactions, giving unchanged acid (0·48 g.), m. p. and mixed m. p. 148°. The ethereal layer containing neutral material yielded a greenish oil which solidified and was crystallised from light petroleum (b. p. 60—80°), giving 2-*hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI) as rectangular prisms (0·62 g.), m. p. 76—80°. A second crystallisation raised the m. p. to 80—81° (Found: C, 75·4; H, 8·5. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

The mother-liquors and the residue after separation of the hydroxychroman were distilled, giving 2 : 4 : 4 : 7-*tetramethylchromen* (XVIII) (0·149 g.), b. p. 46—47°/0·1 mm. (Found: C, 83·5; H, 8·8. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%). It slowly reduced a cold solution of potassium permanganate in acetone, and instantly decolourised a solution of bromine in chloroform.

2 : 3 : 5 : 6 : 8-*Pentabromo*-2 : 4 : 4 : 7-*tetramethylchroman.*—(*a*) 2 : 4 : 4 : 7-Tetramethylchromen (XVIII) (0·123 g.) was treated at room temperature with bromine (1 c.c.), a vigorous reaction occurring. After 2 hours the semi-solid product was crystallised twice from light petroleum (2 c.c.; b. p. 60—80°) containing a trace of benzene (charcoal), giving 2 : 3 : 5 : 6 : 8-*pentabromo*-2 : 4 : 4 : 7-*tetramethylchroman* as clusters of nacreous blades, m. p. 167° (*ca.* 50%) (Found: C, 26·9; H, 1·9; Br, 68·0. $C_{13}H_{12}OBr_5$ requires C, 26·7; H, 2·2; Br, 68·4%).

(*b*) 2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) (0·05 g.) in chloroform (0·5 c.c.) was treated with bromine (0·2 c.c.) at room temperature. Next day, the residue after evaporation to dryness was crystallised twice from light petroleum (2 c.c.; b. p. 60—80°; charcoal), giving the pentabromotetramethylchroman, m. p. and mixed m. p. 166° (yield *ca.* 48%).

Methylation of 2-*Hydroxy*-2 : 4 : 4 : 7-*tetramethylchroman* (XVI). 4-(2-*Methoxy*-4-*methylphenyl*)-4-*methylpentan*-2-*one* (XVII).—The hydroxychroman (XVI) (0·400 g.) was boiled with a solution of sodium hydroxide (8 g.) in water (10 c.c.) for 5 minutes, then cooled, and methanol (5 c.c.) added. Methyl sulphate (5 c.c.) was then added during 5 minutes, boiling continued for 15 minutes, water (50 c.c.) added, and the solution extracted with ether (2 × 20 c.c.), giving an oil (0·260 g.), b. p. 132°/4 mm. This oil was dissolved in ethanol (5 c.c.) and added at *ca.* 60° to a solution of 2 : 4-dinitrophenylhydrazine (0·300 g.) in ethanol (10 c.c.) and concentrated sulphuric acid (2 c.c.). The solution was boiled for a few minutes, then cooled, and the solid finally crystallised from ethanol (15 c.c.), giving deep orange needles (0·380 g.), m. p. 143° (Found: C, 60·4; H, 6·1. Calc. for $C_{20}H_{24}O_5N_4$: C, 60·0; H, 6·0%) alone or mixed with a specimen similarly prepared from 4-(2-methoxy-4-methylphenyl)-4-methylpentan-2-one (XVII) which had been synthesised by a different method (Part VI, *loc. cit.*). The m. p. of 138° previously recorded for this 2 : 4-dinitrophenylhydrazone is that of a second form crystallising in thin plates which was prepared at room temperature.

2-*Ethoxy*-2 : 4 : 4 : 7-*tetramethylchroman.*—2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) (0·400 g.) in dry ethanol (5 c.c.) was saturated with hydrogen chloride and then boiled for

4 hours. The diluted product yielded to ether *2-ethoxy-2 : 4 : 4 : 7-tetramethylchroman* as a viscous oil (0·201 g., 44%), b. p. 74°/0·2 mm. (Found: C, 77·4; H, 9·0. $C_{15}H_{22}O_3$ requires C, 76·9; H, 9·4%).

2-Amino-2 : 4 : 4 : 7-tetramethylchroman (XX).—Bromine (0·8 g.) was added to a solution of potassium hydroxide (1·12 g.) in water (11·2 c.c.) at −10°. 2 : 4 : 4 : 7-Tetramethylchroman-2-carboxyamide (XIX) (1·16 g.; Baker, Curtis, and McOmie, Part VI, *loc. cit.*) in dioxan (7 c.c.) was now added with efficient stirring to the solution at 0°, and stirring was continued at 0° for 15 minutes and then for 1½ hours at 80°, and the cooled solution was diluted and extracted with ether (2 × 30 c.c.). The extract was shaken with excess of dilute hydrochloric acid, and the acid layer when neutralised gave an oil which solidified (the ether yielded unchanged amide, 0·197 g., m. p. 146—147°). After being dried *in vacuo* this *2-amino-2 : 4 : 4 : 7-tetramethylchroman* (XX) (0·497 g.) had m. p. 74°, raised to 76° by recrystallisation from aqueous methanol (charcoal) (Found: C, 75·9; H, 9·3; N, 6·7. $C_{13}H_{19}ON$ requires C, 76·1; H, 9·3; N, 6·8%). The amine (XX) (0·04 g.) in acetic acid (0·2 c.c.) and acetic anhydride (0·5 c.c.) was kept for 1½ hours, then diluted and shaken; the solid was collected, and finally crystallised from benzene–light petroleum (b. p. 60—80°) (2 c.c.). *2-Acetamido-2 : 4 : 4 : 7-tetramethylchroman* separated in fine needles (0·031 g.), m. p. 134° (Found: C, 72·5; H, 8·4; N 5·85. $C_{15}H_{21}O_2N$ requires C, 72·9; H, 8·5; N, 5·7%).

2-Hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI) *from 2-Amino-2 : 4 : 4 : 7-tetramethylchroman* (XX).—Sodium nitrite (0·024 g.) in water (2 c.c.) was added to the amine (XX) (0·069 g.) in dilute hydrochloric acid (10 c.c.; 10%) at room temperature, and after 6 hours the whole was diluted with water and extracted with ether. The extracts were shaken with hydrochloric acid in excess, then with water, dried, and distilled, giving an oil which was dissolved in light petroleum (b. p. 60—80°) (charcoal); the solution was filtered and concentrated to 2 c.c. The resulting solid was sublimed (100°/13 mm.), giving prisms (0·007 g.), m. p. 80° not depressed by a specimen of 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman (XVI), m. p. 80—81°.

Crystalline Complexes formed by the Flavans (VI) *and* (VII).—These *complexes* were prepared by dissolving the flavan in light petroleum (b. p. 40—60°) and adding the other component of the complex (see Part VII, *loc. cit.*). In connection with the annexed list it is to be understood that, except for those mentioned, complexes are not formed with organic solvents usually found in the laboratory, with other solvents mentioned in this list, or with solvents listed in Part VII as forming complexes with 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (I).

Crystalline complexes formed by flavans (VI) *and* (VII).

Component	M. p. (dissociation)	Ratio, flavan : component	Analyses: Found, % (required % in parentheses) Carbon	Hydrogen	Nitrogen
	2′-Hydroxy-2 : 4 : 4-trimethylflavan (VI) *				
Dioxan	142—144°	2 : 1	76·7 (76·9)	7·6 (7·7)	—
Morpholine	146—148	2 : 1	76·7 (77·0)	7·9 (7·9)	—
	2′-Hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan (VII) †				
Tetrahydrofuran	77—79	1 : 1	78·2 (78·3)	8·8 (8·7)	—
Morpholine	109—111	1 : 1	75·2 (75·2)	8·6 (8·6)	3·7 (4·0)
Pyridine	101—103	1 : 1	80·4 (80·0)	7·7 (7·7)	—
Piperidine	100—102	1 : 1	—	—	3·6 (3·7)
*cyclo*Hexylamine	69—71	1 : 1	—	—	3·5 (3·5)

* Crystalline complexes (uncharacterised) are also formed with diethylamine, di*iso*propylamine, aniline, *cyclo*hexylamine, pyridine, and 2-bromopyridine.

† Complexes are also formed with dioxan and diethylamine (already described in this paper), di-*n*-propylamine, di*iso*propylamine, di-*n*-butylamine, di*iso*butylamine, 3-methylpyridine, 4-methylpyridine, 2 : 6-dimethylpyridine.

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329. *Steroids. Part I. A New Preparation of the Cholesteryl Halides.*

By C. W. Shoppee and G. H. R. Summers.

A new route leading to cholesteryl chloride, bromide, and iodide is described.

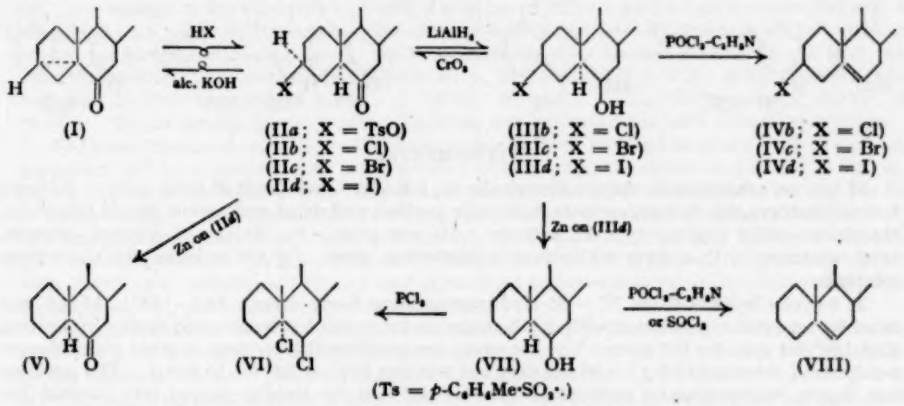
Two methods are available for the preparation of cholesteryl halides from cholesterol. One of these is the direct replacement of the 3β-hydroxyl group by phosphorus pentachloride (Mauthner, *Monatsh.*, 1894, **15**, 87), by thionyl chloride (Diels, Abderhalden, and Blumberg, *Ber.*, 1904, **37**, 3092; 1911, **44**, 287; Daughensbaugh and Allison, *J. Amer. Chem. Soc.*, 1929, **51**, 3665), or by hydrogen chloride (this paper), leading to cholesteryl chloride, or by use of phosphorus tribromide (Kolm, *Monatsh.*, 1912, **33**, 447; Lieb, Winkelmann, and Köppl, *Annalen*, 1934, **509**, 214) or thionyl bromide (Bide, Henbest, Jones, and Wilkinson, *J.*, 1948, 1787), leading to cholesteryl bromide. The other method involves the conversion of cholesterol into 6β-hydroxy-, 6β-methoxy-, or 6β-acetoxy-3 : 5-*cyclo*cholestane [formerly termed *i*-cholesterol, *i*-cholesteryl methyl ether and acetate] (Shoppee and Summers, to be published) or into 3 : 5-*cyclo*cholest-6-ene [formerly termed *i*-cholestadiene] (Riegel, Hager, and Zenitz, *J. Amer. Chem. Soc.*, 1946, **68**, 2562), which by treatment with hydrogen chloride, hydrogen bromide, or hydrogen iodide in acetic acid at 20° readily rearrange to furnish cholesteryl chloride, bromide, or iodide (Beynon, Heilbron, and Spring, *J.*, 1936, 907; 1937, 1459; Wallis and Ford, *J. Amer. Chem. Soc.*, 1937, **59**, 1415).

In connection with other investigations, the hitherto unknown *epi*cholesteryl chloride was required. Direct replacement by chlorine of the 3α-hydroxyl group of *epi*cholesterol proving unsatisfactory, and the 3 : 5-*cyclo*steroid rearrangement appearing to be β-stereospecific and so inapplicable, we have devised a new route to cholesteryl chloride, bromide, and iodide, and have applied it to the preparation of *epi*cholesteryl chloride and bromide (see following paper).

The starting material chosen was 3 : 5-*cyclo*cholestan-6-one [formerly called "cholesten-6-one" and *i*-cholestanone] (I) (Windaus and Dalmer, *Ber.*, 1919, **52**, 162; Windaus and von Staden, *ibid.*, 1921, **54**, 1059; Ford, Chakravorty, and Wallis, *J. Amer. Chem. Soc.*, 1938, **60**, 413; Heilbron, Hodges, and Spring, *J.*, 1938, 759), which was prepared by treatment of the toluene-*p*-sulphonate of 3β-hydroxycholestan-6-one (II*a*) with alcoholic potassium hydroxide (Dodson and Riegel, *J. Org. Chem.*, 1948, **13**, 424).

The ketone (I) is quantitatively converted by hydrogen chloride in acetic acid at 20° into 3β-chlorocholestan-6-one (II*b*) (Ford, Chakravorty, and Wallis, *loc. cit.*); this change involves inversion of configuration at $C_{(3)}$, and we find that by use respectively of hydrogen bromide and hydrogen iodide under appropriate conditions there are produced similarly 3β-bromo- (II*c*), and 3β-iodo-cholestan-6-one (II*d*). The 3β-iodo-ketone (II*d*) is reduced by zinc to cholestan-6-one (V) ["heterocholestanone"] (Windaus and Dalmer, *loc. cit.*; Windaus, *Ber.*, 1920, **53**, 488). The 3β-halogeno-ketones (II*b*—*d*) by reduction with lithium aluminium hydride at low temperature (0—20°) afford respectively 3β-chloro- (III*b*), 3β-bromo- (III*c*) and 3β-iodo-cholestan-6β-ol (III*d*), which are unaccompanied by appreciable amounts of the 6α-epimerides and are reconverted into the appropriate 3β-halogeno-ketones (II) by oxidation with chromium trioxide. The 3β-chloro-alcohol (III*b*) by reduction with sodium and amyl alcohol, or better the 3β-iodo-alcohol (III*d*) by reduction with zinc, gives cholestan-6β-ol, m. p. 82° (VII) [acetate, m. p. 75°; benzoate, m. p. 79°]. Plattner, Petrzilka, and Lang (*Helv. Chim. Acta*, 1944, **27**, 513) by reduction of 5α : 6α-epoxycholestane isolated cholestan-5α-ol but could not obtain the accompanying cholestan-6-ol (which should be the β-epimeride); the acetate, m. p. 75°, of a cholestan-6-ol has previously been described by Reich and Lardon (*ibid.*, 1946, **29**, 671) without assignment of configuration at $C_{(6)}$. The compound described in Elsevier's "Encyclopædia" (Vol. XIV, p. 66) as cholestan-6β-ol is in fact cholestan-6α-ol, m. p. 130° [acetate, m. p. 95°; benzoate, m. p. 103°], obtained from cholestan-6-one by reduction with sodium and ethanol (Tschesche, *Ber.*, 1932, **65**, 1842); cholestan-6α-ol. m. p. 127—129°, although described as cholestan-6β-ol,

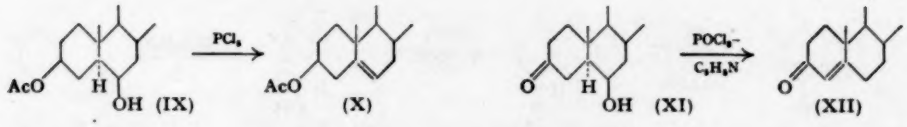
was also the substance used by Karrer, Asmis, Sareen, and Schwyzer (*Helv. Chim. Acta*, 1951, **34**, 1022) and was characterised as the toluene-*p*-sulphonate, m. p. 108·5—110° (which we have also prepared) (private communication from Prof. Karrer).



It will be seen not only that in the 3β-halogeno-alcohols (III*b*—*d*) the 5α-hydrogen atom and the 6β-hydroxyl group possess the *trans*-arrangement, but also that both atom and group are united to carbon atoms of ring B by bonds belonging to the set of six lying in a plane perpendicular to the general plane of ring B and termed polar (Beckett, Pitzer, and Spitzer, *J. Amer. Chem. Soc.*, 1947, **69**, 2488; cf. Hassell and Viervoll, *Acta Chem. Scand.*, 1947, **1**, 149). Thus the four centres 5α-H, $C_{(5)}$, $C_{(6)}$, and 6β-O(H) are coplanar and comply with the conditions for minimisation of the activation energy of a synchronous ionic elimination reaction (E_2) (Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, *J.*, 1948, 2093; cf. Barton, *Experientia*, 1950, **6**, 316; Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 370, 1066; Barton and Rosenfelder, *J.*, 1951, 1048; Barton, Miller, and Young, *ibid.*, p. 2598). Dehydration of the 3β-halogeno-alcohols (III*b*—*d*) proceeds readily with phosphorus oxychloride and pyridine at 20° to give respectively cholesteryl chloride (IV*b*), cholesteryl bromide (IV*c*), and cholesteryl iodide (IV*d*).

It is of interest that, whilst treatment of cholestan-6α-ol with thionyl chloride leads to substitution with retention of configuration and formation of 6α-chlorocholestane, m. p. 151°, $[\alpha]_D$ +51° (Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 371), the epimeric cholestan-6β-ol (VII) with thionyl chloride undergoes dehydration with formation of cholest-5-ene (VIII). Employment of phosphorus pentachloride in the case of cholestan-6α-ol leads to substitution with inversion, to give 6β-chlorocholestane, m. p. 147°, $[\alpha]_D$ −45° (Stange, *Z. physiol. Chem.*, 1933, **220**, 34), but in the case of cholestan-6β-ol this reagent furnishes 5α : 6β-dichlorocholestane (VI), m. p. 119°, $[\alpha]_D$ −29° (cf. Mauthner, *Monatsh.*, 1906, **27**, 421; Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 370). We believe that this compound arises by facile dehydration of cholestan-6β-ol (VII) to cholest-5-ene (VIII) and subsequent *trans*-addition of a molecule of chlorine derived from phosphorus pentachloride by the reaction $PCl_5 \rightleftharpoons PCl_3 + Cl_2$. An analogous equilibrium involving phosphorus trichloride and bromine has been shown to exist in carbon tetrachloride solution at 20° (C. C. Price, unpublished observation): $PCl_3Br_2 \rightleftharpoons PCl_3 + Br_2$. We are greatly obliged to Professor Price, of Notre Dame University, Indiana, for this information which appears to afford a satisfactory explanation for the above conversion of a monohydric alcohol into a dichloride. A further example appears to be the conversion of cholesterol, by grinding it with phosphorus pentachloride, into cholesteryl chloride, whereas in the presence of benzene cholesteryl chloride dichloride is formed (Pirrone, *Gazzetta*, 1932, **62**, 63). On the other hand it may be noted that the 3-acetate (IX) of cholestane-3β : 6β-diol with phosphorus pentachloride in benzene gave cholesteryl acetate (X) and not cholesteryl acetate dichloride (Barton and Rosenfelder, *J.*, 1949, 2459). Treatment of 6β-

hydroxycholestan-3-one (XI) with phosphorus oxychloride and pyridine probably yields cholest-5-en-3-one as the initial reaction product although the material isolated under our conditions was cholest-4-en-3-one (XII).



Experimental

M. p.s were determined thermo-electrically on a Kofler block (limit of error ±2°). Solvents for chromatographic operations were rigorously purified and dried and, unless stated otherwise, aluminium oxide (Spence type H, activity ~II) was used. For drying of ethereal extracts, brief treatment with anhydrous sodium sulphate was used. [α] are recorded for chloroform solutions.

3 : 5-cyclo*Cholestan*-6-*one* (I).—3β-Hydroxycholestan-6-one (m. p. 142—143°; 15 g.) was dried by repeated evaporation with dry benzene under reduced pressure, and finally by heating it at 100°/0·1 mm. for 0·5 hour. The ketone in dry pyridine (10 c.c.) was treated with toluene-*p*-sulphonyl chloride (12·3 g.), and the deep red solution kept at 25° for 15 hours. The pyridine was largely removed under reduced pressure at 40° and the residue poured into ice-cold 2N-hydrochloric acid and set aside for 0·5 hour. The product was extracted with chloroform–ether, and the extract washed to neutrality with water, 2N-sodium hydrogen carbonate, and water. Evaporation yielded a thick crust of 3β-toluene-*p*-sulphonyloxycholestan-6-one (II*a*), which was recrystallised from acetone, to give needles, m. p. 186° (decomp.), $[\alpha]_D$ −5° ± 1° (*c*, 1·133) (Riegel and Dodson, *J. Org. Chem.*, 1948, **13**, 424, give m. p. 169—179°, $[\alpha]_D$ −5·5° ± 0·7°); the yield after repeated crystallisation was 16·7 g. This material was converted by the method of Dodson and Riegel (*loc. cit.*) into 3 : 5-*cyclo*cholestan-6-one, which was finally purified by filtration of a pentane solution through a column of aluminium oxide and had m. p. 96—97°.

3β-*Chlorocholestan*-6β-*ol* (III*b*).—3β-Chlorocholestan-6-one (II*b*) (m. p. 129—130°; 1·47 g. in 100 c.c. of dry ether) was added dropwise during 0·25 hour to an ice-cold solution of lithium aluminium hydride (0·5 g.) in ether (150 c.c.). The solution was poured into ice-water, and the ethereal layer washed with 2N-sulphuric acid, sodium hydrogen carbonate solution, and water. After drying, removal of the ether yielded 3β-*chlorocholestan*-6β-*ol* as an oil (1·34 g.) which crystallised from pentane in needles, m. p. 96°, $[\alpha]_D$ +14·5° ± 2° (*c*, 4·10) (Found, after drying at 20°/0·01 mm. for 20 hours: C, 76·6; H, 11·0. $C_{27}H_{47}OCl$ requires C, 76·6; H, 11·1%). It gave no colour with tetranitromethane in chloroform. 3β-Chlorocholestan-6β-ol (250 mg.) in acetic acid (5 c.c.) was treated with a 2% solution of chromium trioxide in acetic acid (2 c.c.), and the mixture left at 20° for 12 hours. Excess of chromium trioxide was destroyed with methanol, and, after dilution with water, the product was extracted with ether. The ethereal extract was washed with water, 2N-sodium carbonate, and water, then dried, and evaporated to yield an oil (237 mg.) which crystallised from methanol in needles, m. p. 127—128°, undepressed by admixture with an authentic specimen of 3β-chlorocholestan-6-one which had $[\alpha]_D$ −1° ± 1·5° (*c* = 1·17).

Cholesteryl Chloride (IV*b*).—(*a*) Phosphorus oxychloride (0·5 c.c.) was added with ice-cooling to a solution of 3β-chlorocholestan-6β-ol (108 mg.) in dry pyridine (6 c.c.) and left at 20° overnight. The reaction mixture was poured into ice-water, and the product extracted with ether. The ethereal extract after the usual purification and drying yielded an oil (79 mg.) which was further purified by filtration of a pentane solution through a column of aluminium oxide. The colourless oil readily crystallised (exhibiting anisotropic transformation colours) and separated from acetone–methanol as plates, m. p. 94—96°, undepressed on admixture with an authentic specimen.

(*b*) Cholesterol (2·2 g.) (m. p. 148°; commercial material purified by successive bromination, crystallisation of cholesterol dibromide from ether–ethanol, and debromination with sodium iodide) in absolute methanol (200 c.c.) was heated under reflux for 7 hours with concentrated hydrochloric acid (20 c.c.). The yellow solution was reduced to half its volume in a vacuum, poured into water, and extracted with ether, and the extract dried and evaporated to give a crystalline solid. This was chromatographed on aluminium oxide (70 g.), and the chromatogram eluted with pentane and pentane–benzene (19 : 1) until no further material was obtained.

The oil (76 mg.) so obtained crystallised from ether–methanol as needles, m. p. 95—96° undepressed on admixture with a genuine specimen of cholesteryl chloride.

3β-*Bromocholestan*-6β-*ol* (III*c*).—3β-Bromocholestan-6-one (m. p. 123—125°; 550 mg.), prepared by treatment of an acetic acid solution of 3 : 5-*cyclo*cholestan-6-one with 48% hydrobromic acid, was treated in dry ether (50 c.c.) with a solution of lithium aluminium hydride (220 mg.) in ether (100 c.c.). The mixture was cooled in an ice-bath and after 0·25 hour was worked up as described for 3β-chlorocholestan-6β-ol. 3β-*Bromocholestan*-6β-*ol* was isolated as an oil (550 mg.) which crystallised from methanol as prisms, m. p. 95°, $[\alpha]_D$ +14° ± 2° (*c*, 3·97) (Found,* after drying at 20°/0·01 mm. for 16 hours: C, 70·95; H, 10·7. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·1%). The substance gave a positive Beilstein test but no colour with tetranitromethane.

3β-*Bromocholestan*-6-*one* (II*c*).—3β-Bromocholestan-6β-ol (70 mg.) in acetic acid (3 c.c.) was warmed to 50° for 5 minutes with a 2% solution of chromium trioxide in acetic acid (3 c.c.) and the whole then poured into water; the product was extracted with ether, and the extract purified in the usual way. 3β-Bromocholestan-6-one was obtained as needles (from acetic acid), m. p. 123° undepressed on admixture with an authentic specimen, which had $[\alpha]_D$ +3° ± 1° (*c*, 4·29).

Cholesteryl Bromide (IV*c*).—3β-Bromocholestan-6β-ol (III*d*) (200 mg.) in pyridine (6 c.c.) with phosphorus oxychloride (2 c.c.) and subsequent treatment as for (III*c*) yielded 3β-bromocholest-5-ene, m. p. 96—98°, in quantitative yield.

3β-*Iodocholestan*-6-*one* (II*d*).—3 : 5-*cyclo*Cholestan-6-one (1·7 g.) was dissolved in pure acetic acid (25 c.c.) and treated with 54% hydriodic acid (5 c.c.). The turbid solution was made clear by the addition of ether; almost immediately needles formed on the surface of the solution and after storage overnight a thick cluster of very long needles had formed at the bottom of the flask. The supernatant liquid was decanted, the needles were washed with acetic acid, and the washings combined with the main solution. This was diluted with water and the product extracted with ether–benzene. The extract was worked up in the usual way and a red-violet oil was obtained which solidified on being moistened with acetic acid. 3β-*Iodocholestan*-6-*one* crystallised from acetic acid in needles, m. p. 137—138°, $[\alpha]_D$ +8° ± 2° (*c*, 4·13) (total yield 1·72 g.) (Found, after drying at 20°/0·05 mm. for 16 hours: C, 63·5; H, 8·75. $C_{27}H_{45}OI$ requires C, 63·3; H, 8·8%). The compound gave a positive Beilstein test.

3β-*Iodocholestan*-6β-*ol* (III*d*).—3β-Iodocholestan-6-one (1·45 g.) in ether (120 c.c.) was shaken with a solution of lithium aluminium hydride (0·5 g.) at 0° for 10 minutes. The solution was poured into ice-water, and the ethereal layer separated and washed with 4N-sulphuric acid, and then water to neutrality. Evaporation of the solvent afforded a colourless oil (1·5 g.), which crystallised on cooling. Recrystallisation from ethanol or methanol–acetone gave 3β-*iodocholestan*-6β-*ol* as needles, m. p. 109—110°, $[\alpha]_D$ +15° ±3° (*c*, 4·79) (Found, after drying at 20°/0·05 mm. for 8 hours: C, 63·0; H, 9·2. $C_{27}H_{47}OI$ requires C, 62·9; H, 9·2%). The substance was saturated to tetranitromethane. 3β-Iodocholestan-6β-ol (20 mg.) was dissolved in acetic acid (1 c.c.), treated with a 2% solution of chromium trioxide in acetic acid (1 c.c.), and warmed at 40° for 10 minutes. The solid neutral product, isolated in the usual way, consisted of 3β-iodocholestan-6-one, m. p. 137°.

Cholesteryl Iodide (IV*d*).—3β-Iodocholestan-6β-ol (100 mg.) in pyridine (4 c.c.) was treated with phosphorus oxychloride (1 c.c.) and left overnight at room temperature. Working up as described above gave an oil which solidified in rosettes and crystallised from ethanol in long plates (84 mg.), m. p. 105—106°, undepressed on admixture with authentic 3β-iodocholest-5-ene.

Cholestan-6-*one* (V).—3β-Iodocholestan-6-one (25 mg.) in glacial acetic acid (5 c.c.) was heated under reflux for 0·25 hour with zinc dust (70 mg.). The acetic acid was removed under reduced pressure, the crystalline residue extracted with ether, and the extract filtered from the zinc dust; working up in the usual way gave a colourless oil, which crystallised from methanol in plates (16 mg.), m. p. 97—98°, undepressed on admixture with genuine cholestan-6-one.

Cholestan-6β-*ol* (VII).—Reduction of 3β-iodocholestan-6β-ol with zinc dust in a similar manner gave cholestan-6β-ol, m. p. 81°, in quantitative yield.

Cholest-5-*ene* (VIII).—Cholestan-6β-ol (50 mg.) in pyridine (1 c.c.) was treated with phosphorus oxychloride (3 drops) at 0° and left overnight at 20°. The product, isolated in the usual way, was identical with cholest-5-ene, m. p. 89°, prepared by reduction of cholesteryl chloride with sodium–amyl alcohol. Thionyl chloride in pyridine at 20° gave the same product.

5α : 6β-*Dichlorocholestane* (VI).—Cholestan-6β-ol (74 mg.) was ground with phosphorus pentachloride (200 mg.) and benzene (1 c.c.) for 10 minutes. The mixture became a brilliant purple.

* We are unable to record a good analysis for this substance, a second set of figures being C, 71·2; H, 10·2%.

After the whole had been warmed with water 5α : 6β-*dichlorocholestane* was isolated as an oil which crystallised from methanol as leaflets, m. p. 114—116°, $[\alpha]_D$ −29° ± 2° (*c*, 1·830) (Found, after drying at 80°/0·01 mm. for 2 hours: C, 73·6; H, 10·3. $C_{27}H_{46}Cl_2$ requires C, 73·5; H, 10·5%). The compound gave a positive Beilstein test and was saturated to tetranitromethane.

Cholest-4-en-3-one.—6β-Hydroxycholestan-3-one (m. p. 184°; 176 mg.) in pyridine (4 c.c.) was treated at 0° with phosphorus oxychloride (1 c.c.), and the mixture left at 20° overnight. An oily product was isolated which solidified on being rubbed with methanol. Chromatography on neutral alumina * gave, by elution with pentane, cholest-4-en-3-one, m. p. 79—81° (146 mg.).

One of us (C. W. S.) acknowledges gratefully a grant from the Royal Society which has partly defrayed the expense of the work described in this and the following paper, whilst the other (G. H. R. S.) acknowledges the award of a Postgraduate Studentship by the University of Wales and a grant from the Department of Scientific and Industrial Research which enabled him to participate in these investigations. Microanalyses are by Dr. Weiler and Dr. Strauss, Oxford.

UNIVERSITY COLLEGE, SWANSEA, THE UNIVERSITY OF WALES. [*Received, February 7th*, 1952.]

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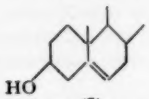
330. *Steroids. Part II.*† *The Preparation of* epi*Cholesteryl Chloride and Bromide.*

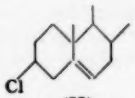
By C. W. SHOPPEE and G. H. R. SUMMERS.

The preparation of *epi*cholesteryl chloride and *epi*cholesteryl bromide from the corresponding 3α-halogenocholestan-6β-ols is described.

IT has been shown (Shoppee, *J.*, 1946, 1147) that the conversion of cholesterol (I) into cholesteryl chloride (II) (or bromide) occurs with preservation of configuration at $C_{(3)}$. It seemed possible that conditions might be found for the analogous conversion of *epi*cholesterol (III) into *epi*cholesteryl chloride (IV) (or bromide). Despite numerous experiments (to be described subsequently in another connexion) such conditions have not been found, but we have been able to prepare *epi*cholesteryl chloride (IV*a*) and *epi*cholesteryl bromide by a suitable modification of the route, described in the preceding paper, leading to the cholesteryl halides (as II).



(I)



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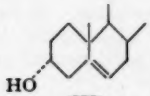

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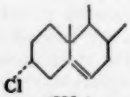


(IV*a*)

3β-Hydroxycholestan-6-one (V) was converted by treatment with phosphorus pentachloride into 3α-chlorocholestan-6-one (VI*a*) (Windaus and Stein, *Ber.*, 1904, **37**, 3699; Windaus and von Staden, *ibid.*, 1921, **54**, 1059). The configuration at $C_{(3)}$ of (VI*a*) has been proved (Shoppee, *J.*, 1948, 1032), and by reduction with lithium aluminium hydride at 0—20° this compound furnished 3α-chlorocholestan-6β-ol (VII*a*), unaccompanied by any detectable quantity of the 6α-epimeride and reconverted into the 3α-chloro-ketone by chromium trioxide. Dehydration of the 3α-chloro-alcohol (VII*a*) with phosphorus oxychloride and pyridine at 20° readily gave *epi*cholesteryl chloride (IV*a*).

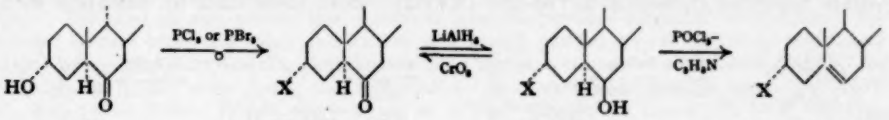
Similarly, by use of phosphorus pentabromide there was obtained 3α-bromocholestan-6-one (VI*b*), reduced to 3α-bromocholestan-6β-ol (VII*b*), which was dehydrated to yield *epi*cholesteryl bromide (IV*b*).

The hydroxy-ketone (V) has been converted into *epi*cholesteryl chloride by two other routes. Reduction with lithium aluminium hydride gives cholestane-3β : 6β-diol (VIII)

* Aluminium oxide (Spence, type H) was warmed for 1 hour on a steam-bath with 5% nitric acid, filtered off, and washed until the filtrate was free from NO_3^-. The material was then extracted twice with boiling methanol for 1 hour, and reactivated at 250°/10 mm. for 1 hour.

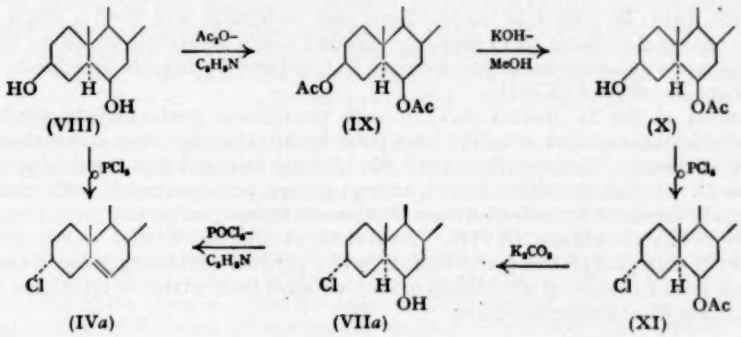
† Part I, preceding paper.

(Marker and Krueger, *J. Amer. Chem Soc.*, 1940, **62**, 79; Plattner and Lang, *Helv. Chim. Acta*, 1944, **27**, 1872) as the main product, accompanied by some cholestane-3β : 6α-diol (Windaus, *Ber.*, 1917, **50**, 133; Barton and Rosenfelder, *J.*, 1951, 2381). The 3β : 6β-diol



(V) (VI*a*; X = Cl) (VI*b*; X = Br) (VII*a*; X = Cl) (VII*b*; X = Br) (IV*a*; X = Cl), m. p. 107°, $[\alpha]_D$ −3°. (IV*b*; X = Br), m. p. 105°, $[\alpha]_D$ +5°.

(VIII), when treated with phosphorus pentachloride, undergoes substitution with inversion of configuration at $C_{(3)}$, and subsequent dehydration gives *epi*cholesteryl chloride (IV*a*) accompanied by some cholesta-3 : 5-diene. Alternatively, the 3β : 6β-diol (VIII) may be converted into the 3β : 6β-diacetoxy-compound (IX), which by partial hydrolysis affords the 6β-acetoxycholestan-3β-ol (Plattner and Lang, *loc. cit.*); this, on treatment with phosphorus pentachloride, undergoes replacement with inversion of configuration at $C_{(3)}$, to yield 3α-chloro-6β-acetoxycholestane (XI), which is hydrolysed by potassium carbonate at 20° to 3α-chlorocholestan-6β-ol (VII*a*); this in turn is dehydrated by phosphorus oxychloride and pyridine to *epi*cholesteryl chloride (IV*a*).



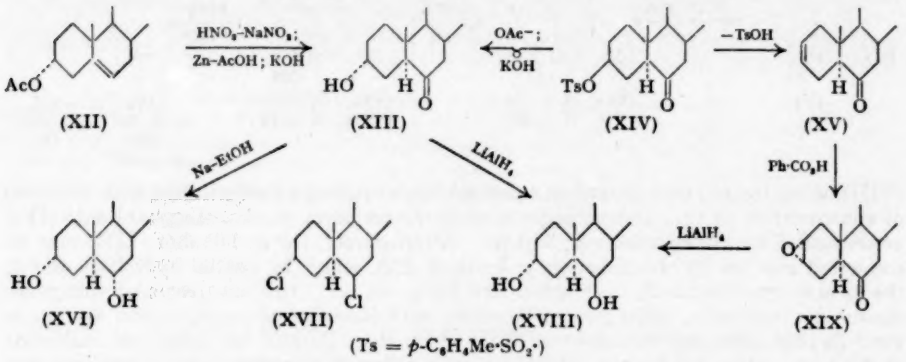
(VIII) (IX) (X) (IV*a*) (VII*a*) (XI)

Both *epi*cholesteryl chloride and bromide are stable crystalline substances; in the Rosenheim test, which depends on the formation of a diene system, both give an immediate pale pink colour which rapidly deepens to red. Whereas cholesteryl chloride and bromide by hydrogenation furnish good yields of 3β-chloro- and 3β-bromo-cholestane respectively, *epi*cholesteryl chloride gives only a little 3α-chlorocholestane accompanied by much cholestane. Other reactions of the *epi*cholesteryl halides will be described later.

The conversion of cholestane-3β : 6β-diol (VIII) into *epi*cholesteryl chloride (IV*a*) by treatment with phosphorus pentachloride may be contrasted with the behaviour of cholestane-3β : 6α-diol with the same reagent to furnish 3α : 6β-dichlorocholestane (Windaus, *Ber.*, 1917, **50**, 133) and compared with its conversion as the 3β : 6β-dimethanesulphonate into cholesteryl acetate by treatment with silver acetate in acetic acid (Reich and Lardon, *Helv. Chim. Acta*, 1946, **29**, 671). In the first-named reaction, substitution (S_N2) with inversion of configuration at $C_{(3)}$ precedes ionic 5 : 6-elimination ($E2$). In the last-named transformation, the ionic 5 : 6-elimination reaction precedes the substitution reaction (S_N1) at $C_{(3)}$, which, by intervention of the π-electrons so provided, proceeds with preservation of configuration.

It seemed of interest to examine the reactions of cholestane-3α : 6α-diol (XVI) and -3α : 6β-diol (XVIII) with phosphorus pentachloride. These diols were obtained from 3α-hydroxycholestan-6-one (XIII), which was prepared (*a*) from *epi*cholesteryl acetate (XII) by successive nitration, reduction, and hydrolysis, and (*b*) from 3β-toluene-*p*-

sulphonyloxycholestan-6-one (XIV) by acetolysis and subsequent hydrolysis [cholest-2-en-6-one (XV) was also formed]. Reduction of the 3α-hydroxy-ketone (XIII) with sodium and ethanol gave cholestane-3α : 6α-diol (XVI), whilst use of lithium aluminium hydride furnished cholestane-3α : 6β-diol (XVIII). Both these diols by oxidation with



(Ts = *p*-$C_6H_4Me{\cdot}SO_2$·)

chromium trioxide gave cholestane-3 : 6-dione; the structure of the 3α : 6β-diol was also confirmed by an alternative preparation. It has been shown (Plattner and Fürst, *Helv. Chim. Acta*, 1949, **32**, 275) that cholest-2-ene and perbenzoic acid yield a single 2α : 3α-epoxide; cholest-2-en-6-one (XV) similarly affords a single substance, which we formulate by analogy as 2α : 3α-epoxycholestan-6-one (XIX), reduced by lithium aluminium hydride to cholestane-3α : 6β-diol (XVIII).

Treatment of the 3α : 6β-diol (XVIII) with phosphorus pentachloride resulted in a double dehydration reaction, whereby both polar hydroxyl groups were eliminated to give cholesta-3 : 5-diene. Windaus (*Ber.*, 1917, **50**, 133) has reported that the doubly epimeric cholestane-3β : 6α-diol, in which both hydroxyl groups are equatorial, with phosphorus pentachloride furnishes by substitution a dichlorocholestane, m. p. 128°, which we regard as 3α : 6β-dichlorocholestane (XVII). Treatment of the 3α : 6α-diol (XVI) (3, polar; 6, equatorial) with phosphorus pentachloride gave a product containing halogen and eluted by pentane from a column of aluminium oxide; we have been unable to crystallise this but it may contain 6β-chlorocholest-2-ene.

Experimental

For general experimental directions see preceding paper. Microanalyses are by Drs. Weiler and Strauss, Oxford.

3α-Chlorocholestan-6-one (VI*a*).—Freshly sublimed phosphorus pentachloride (8 g.) was added in small portions during 1·5 hours to a solution of 3β-hydroxycholestan-6-one (4 g.) in pure dry chloroform (200 c.c.) at 0°, containing a suspension of calcium carbonate (5 g.). After being shaken at 20° overnight, the mixture was poured into water and extracted with ether, and the extract washed with water, 2N-sodium carbonate, and water, dried, and evaporated. 3α-Chlorocholestan-6-one (4·1 g.) was obtained as needles (from acetone), m. p. 181°.

3α-Chlorocholestan-6β-ol (VII*a*).—3α-Chlorocholestan-6-one (VI*a*) (2 g. in 200 c.c. of dry ether) was added dropwise during 0·25 hour to an ice-cold solution of lithium aluminium hydride (1·2 g.) in ether (300 c.c.). The solution was poured into ice-water, and the ethereal solution washed with 2N-sulphuric acid, sodium hydrogen carbonate solution, and water. After drying, removal of the ether yielded 3α-chlorocholestan-6β-ol as an oil (1·94 g.) which crystallised from methanol in long needles, double m. p. 96° and 108°, $[\alpha]_D$ +13° ±2° (*c*, 4·35) (Found, after drying at 60—70°/0·05 mm. for 1 hour: C, 76·9; H, 11·3. $C_{27}H_{47}OCl$ requires C, 76·6; H, 11·1%), which gave no colour with tetranitromethane in chloroform. 3α-Chlorocholestan-6β-ol (76 mg.) was treated in acetic acid (3 c.c.) with a 2% solution of chromium trioxide in acetic acid (2 c.c.), and the mixture left at 20° overnight. Excess of chromium trioxide was destroyed with methanol and, after dilution with water, the product was extracted with ether. The ethereal extract, after the usual washing and drying, by evaporation yielded a

solid (43 mg.), which crystallised from methanol in needles, m. p. 178—180°, undepressed by admixture with an authentic specimen of 3α-chlorocholestan-6-one (VI*a*).

epi*Cholesteryl Chloride* (IV*a*).—Phosphorus oxychloride (0·6 c.c.) was added, with ice-cooling, to a solution of 3α-chlorocholestan-6β-ol (500 mg.) in dry pyridine (5 c.c.) and left at 20° overnight. The mixture was poured into ice-water, and the product extracted with ether. The ethereal extract after the usual purification and drying yielded an oil (467 mg.) which was further purified by filtration of a pentane solution through a column of aluminium oxide. The colourless oil readily crystallised, and recrystallised from acetone as needles, m. p. 105—107° $[\alpha]_D$ −3°±2° (*c*, 1·930) (Found, after drying at 20°/0·1 mm. for 20 hours: C, 79·6; H, 11·4. $C_{27}H_{45}Cl$ requires C, 79·5; H, 11·2%).

3α-*Bromocholestan-6-one* (VI*b*).—3β-Hydroxycholestan-6-one (m. p. 142°; 1·5 g.) and freshly sublimed phosphorus pentabromide (2 g.) were rubbed together in a mortar for 0·25 hour. The mixture was warmed at 40° with water for 0·5 hour, then cooled, and the product extracted with ether and purified by the usual procedure. Removal of the ether gave 3α-bromocholestan-6-one (640 mg.) which separated from methanol–ether as needles, m. p. 173°, $[\alpha]_D$ +10°±1° (*c*, 1·00) (Found, after drying at 20°/0·1 mm. for 20 hours: C, 69·8; H, 9·55. $C_{27}H_{45}OBr$ requires C, 69·8; H, 9·55%).

epi*Cholesteryl Bromide* (IV*b*).—3α-Bromocholestan-6-one (103 mg.) in ether (10 c.c.) was shaken with lithium aluminium hydride (211 mg.) in ether (50 c.c.) at 0° for 10 minutes. The solution was poured into ice-water, and the ethereal solution separated and purified in the usual way. Evaporation of the ether gave an oil, 3α-bromocholestan-6β-ol (VII*b*), which failed to crystallise. Oxidation of this product with a 2% solution of chromium trioxide in acetic acid yielded 3α-bromocholestan-6-one. 3α-Bromocholestan-6β-ol (44 mg.) in dry pyridine (1 c.c.) at 0° was treated with phosphorus oxychloride (3 drops) and left at 20° overnight; the usual method of isolation of the reaction product gave an oil, which after filtration of a pentane solution through a column of neutral * aluminium oxide gave epi*cholesteryl bromide*, m. p. 103—105°, $[\alpha]_D$ −5°±2° (*c*, 1·234), as needles from acetone (Found, after drying at 15°/0·01 mm. for 20 hours: C, 71·8; H, 10·2. $C_{27}H_{45}Br$ requires C, 72·1; H, 10·1%). The compound gave a positive Beilstein test.

Cholestane-3β : 6β-diol (VIII).—3β-Hydroxycholestan-6-one (2·1 g.) in ether (200 c.c.) was added during 20 minutes to a solution of lithium aluminium hydride (2 g.; commercial material) in dry ether (300 c.c.) at room temperature; gentle refluxing was continued for 1 hour. The mixture was cooled in ice, and ice-cold 2N-sulphuric acid added carefully, followed by a large volume of water. The ethereal solution was washed to neutrality in the usual way, dried, and evaporated, yielding a solid which crystallised from acetone–dioxan as prismatic needles, m. p. 185—190°. Recrystallisation from acetone gave cholestane-3β : 6β-diol (1·82 g.) as needles, m. p. 196°. The mother-liquors yielded a residue, which by crystallisation from ethanol formed crystals, m. p. 214—216°, which did not depress the m. p. of authentic cholestane-3β : 6α-diol.

6β-*Acetoxycholestan-3β-ol* (X).—Cholestane-3β : 6β-diol diacetate (IX) (2·5 g.) was refluxed for 1·5 hours with potassium hydroxide (6·25 g.) in methanol (1500 c.c.). The solution was acidified with concentrated hydrochloric acid, the excess of acid neutralised with ammonia, and the methanol removed under reduced pressure. The neutral oily residue was dried by repeated evaporation with dry benzene and chromatographed on aluminium oxide (100 g.). 6β-Acetoxycholestan-3β-ol was isolated by elution with pentane–benzene mixtures (4 : 1 to 1 : 1) in 75% yield and crystallised from methanol in needles, double m. p. 80° and 128° (Plattner and Lang, *Helv. Chim. Acta*, 1944, **27**, 1872, give m. p. 124—125°). Elution with chloroform gave cholestane-3β : 6β-diol.

3α-*Chlorocholestan-6β-yl Acetate* (XI).—Phosphorus pentachloride (freshly sublimed; 1·4 g.) was added in small portions during 1 hour at 0° to a solution of 6β-acetoxycholestan-3β-ol (500 mg.) in dry chloroform (20 c.c.) containing a suspension of dry calcium carbonate (1 g.). The solution was shaken for 1·5 hours and the temperature allowed to rise to 20°. The reaction mixture was digested with water and shaken for a further hour. The chloroform layer was worked up in the usual manner and evaporated, to give 3α-*chlorocholestan-6β-yl acetate* as an oil (356 mg.) which solidified and was recrystallised from methanol as needles, m. p. 127—129°, $[\alpha]_D$ −16°±2° (*c*, 0·442) (Found, after drying at 25°/0·01 mm. for 5 hours: C, 74·4; H, 10·7. $C_{29}H_{49}O_2Cl$ requires C, 74·9; H, 10·6%). The compound gave a positive Beilstein test. 3α-Chlorocholestan-6β-yl acetate (200 mg.) on treatment with an aqueous methanolic solution of potassium carbonate (20 c.c.; 5% solution) at room temperature for 48 hours gave 3α-chlorocholestan-6β-ol.

* See footnote, p. 1790.

epi*Cholesteryl Chloride* (IV*a*).—Cholestane-3β : 6β-diol (3 g.) in dry chloroform (250 c.c.) was treated with phosphorus pentachloride (5 g.) at 0° during 1·5 hours. The solution was digested with water and vigorously shaken for 1·5 hours. The chloroform layer yielded a neutral oil (2·7 g.) which was chromatographed on neutral aluminium oxide (90 g.), and the column was eluted with pentane. The first eluates contained cholesta-3 : 5-diene, m. p. 79°, undepressed on admixture with a genuine specimen; later pentane eluates yielded *epi*cholesteryl chloride (1·97 g.) identical with the material obtained by the dehydration of 3α-chlorocholestan-6β-ol described above.

3α-*Hydroxycholestan-6-one* (XIII).—(*a*) 3α-Hydroxycholestan-6-one was prepared from 3β-toluene-*p*-sulphonyloxycholestan-6-one (XIV) by the method of Dodson and Riegel (*J. Org. Chem.*, 1948, **13**, 424). The toluene-*p*-sulphonate (14·6 g.), after acetolysis and hydrolysis of the product, yielded a dark red oil; this was chromatographed on a column of aluminium oxide (1250 g.) prepared in pentane. Pentane or pentane–benzene (1 : 1) eluted nothing; benzene (8 × 400 c.c.) eluted cholest-2-en-6-one (4·7 g.) (XV), m. p. 102—104° (from acetone); after ether–benzene (1 : 1; 8 × 400 c.c.) had removed a little oil, ether eluted first (7 × 400 c.c.) 3α-hydroxycholestan-6-one (XIII) (2·3 g.), m. p. 156—160° (from aqueous ethanol), and then (6 × 400 c.c.) 3β-hydroxycholestan-6-one (V), m. p. 140—142°. An ethanolic solution of the mother liquors from (XIII) was treated with a solution of digitonin in warm 96% ethanol; a white precipitate was formed which was allowed to settle out overnight. The precipitate was filtered off and decomposed with warm pyridine, to give in the usual manner 3β-hydroxycholestan-6-one, whilst from the filtrate there was obtained 3α-hydroxycholestan-6-one.

(*b*) *epi*Cholesteryl acetate (XII) (m. p. 85°; 618 mg.) was stirred at 20° for 1 hour with concentrated nitric acid (15 c.c.; *d* 1·42), to which potassium nitrite (265 mg.) was added. The thick creamy suspension was filtered on a sintered-glass crucible and was washed thoroughly with water, and dried in a vacuum for 3 days. The compound was not crystallised but was reduced directly with zinc dust and acetic acid for 1½ hours. The resulting solution was diluted with water and extracted with benzene. The extract after purification gave on evaporation an oil, which solidified when rubbed with methanol. This product after hydrolysis with 5% alcoholic potassium hydroxide yielded a solid (215 mg.), which was chromatographed on aluminium oxide (5 g.) and eluted with ether. Crystallisation from aqueous ethanol gave plates, m. p. 156—159°, undepressed by admixture with 3α-hydroxycholestan-6-one.

Cholestane-3α : 6α-*diol* (XVI).—3α-Hydroxycholestan-6-one (700 mg.) in ethanol (50 c.c.) was heated under reflux with sodium (5·5 g.) for 0·5 hour; excess of sodium was destroyed by the addition of ethanol. The reaction mixture was poured into water and extracted with ether. The ethereal extract after purification yielded *cholestane*-3α : 6α-*diol* as a white solid (653 mg.) which crystallised from ethanol–acetone as needles, which melted at 211° with the formation of small droplets; these gradually crystallised into needles and finally melted at 219—220°, and had $[\alpha]_D$ +43°±3° (*c*, 0·67 in dioxan) (Found, after drying at 20°/0·01 mm. for 12 hours and at 100°/0·01 mm. for 1 hour: C, 79·8; H, 11·8. $C_{27}H_{48}O_2$ requires C, 80·1; H, 11·9%). The acetyl derivative could not be obtained crystalline. The diol by oxidation with chromium trioxide–acetic acid gave cholestane-3 : 6-dione, needles (from acetone), m. p. 171—173°, undepressed on admixture with an authentic specimen.

Cholestane-3α : 6β-*diol* (XVIII).—3α-Hydroxycholestan-6-one (1·3 g.) in dry ether (100 c.c.) was added to a solution of lithium aluminium hydride (0·54 g.) in ether (150 c.c.) at 20°. After 0·5 hour the mixture was poured into ice-water, and the ethereal solution separated and purified by the usual procedure. Removal of the ether gave a yellowish-white solid, which separated from all solvents as a gel and could not be obtained crystalline. On oxidation with chromium trioxide–acetic acid, cholestane-3 : 6-dione, m. p. 171—173°, was formed. Acetylation with acetic anhydride–pyridine at 20° gave an oil, which after filtration of a pentane solution through a column of aluminium oxide gave *cholestane*-3α : 6β-*diol diacetate* which, crystallised from acetone after cooling to −10° for several days, had m. p. 87—89°, $[\alpha]_D$ −17°±3° (*c*, 5·06) (Found, after drying at 20°/0·01 mm. for 12 hours: C, 76·3; H, 10·55. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%).

Cholesta-3 : 5-*diene*.—Cholestane-3α : 6β-diol (200 mg.) in dry pyridine (3 c.c.) was treated at 0° with phosphorus oxychloride (0·4 c.c.), and the mixture left at 20° for 12 hours. The product obtained by working up in the usual way was a neutral oil (140 mg.) which crystallised from acetone as needles, m. p. 78—80°, undepressed by admixture with authentic cholesta-3 : 5-diene.

2α : 3α-*Epoxycholestan-6-one* (XIX).—Cholest-2-en-6-one (XV) (1·53 g.) in chloroform (10 c.c.) was treated with a chloroform solution of perbenzoic acid (14·4 c.c.; 1·1 mols. of per-

benzoic acid), and kept at −10° for 15 hours. The solution was washed successively with potassium iodide solution, 0·01N-thiosulphate, sodium hydrogen carbonate solution, and water. Removal of the chloroform gave a colourless oil (1·47 g.), which by crystallisation from acetone gave 2α : 3α-*epoxycholestan*-6-*one* as plates, m. p. 141—142°, $[\alpha]_D$ −14°±2° (*c*, 3·32) (Found, after drying at 20°/0·01 mm. for 2 hours: C, 81·3; H, 11·2. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%).

2α : 3α-Epoxycholestan-6-one (1·43 g.) in ether (200 c.c.) was reduced at 20° with lithium aluminium hydride (1·2 g. in 500 c.c. of ether) in the usual way. The product was isolated as a gel, which was acetylated with acetic anhydride–pyridine at 20° overnight. The product (1·46 g.), isolated in the usual manner, was chromatographed on a column of aluminium oxide (30 g.) prepared in pentane, and gave cholestane-3α : 6β-diol diacetate, m. p. 87—89° (1·34 g.), by elution with pentane (6 × 100 c.c.).

UNIVERSITY COLLEGE, SWANSEA,
THE UNIVERSITY OF WALES.

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331. *Isomorphous Replacement in Hydrated Salts. Part III.* The Systems* $CdCl_2$–$M^{II}Cl_2$–H_2O (M^{II} = Mg, Mn, Fe^{II}, Cu, *or* Ca), *with a Discussion of Certain Solid Solutions found in these Systems.*

By HENRY BASSETT and ROBERT N. C. STRAIN.

The systems indicated in the title have been examined at 25°, and the existence of the following double salts established: $2CdCl_2,MgCl_2,12H_2O$; $CdCl_2,2MgCl_2,12H_2O$; $4CdCl_2,MnCl_2,10H_2O$; $CdCl_2,CuCl_2,4H_2O$; $CdCl_2,2CaCl_2,12H_2O$; and that of $2CdCl_2,FeCl_2,12H_2O$ has been confirmed qualitatively. Each of these systems shows in addition one or more series of solid solutions. They appear to belong to several types and their nature is discussed. Most interest is attached to the solid solutions crystallising in thin negative hexagonal plates which appears to be a layer-lattice structure between $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$ and $CdCl_2,2NaCl,3H_2O$ as end members. In some cases the $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$ is stable enough to be isolated by itself; in other cases only intergrowths with $CdCl_2,2NaCl,3H_2O$ are obtainable.

WHEN investigating the system $CdCl_2$–$NiCl_2$–H_2O at 25° Bassett and others (Parts I and II, *locc. cit.*) discovered a solid solution crystallising in thin negative hexagonal plates which could be represented by the formula $(Cd,Ni)Cl_2,2{\cdot}5H_2O$, where Cd and Ni can replace one another and where there are 2·5 molecules of water for each atom of metal. This solid solution was observed over only a limited region, which is not surprising, since one end member, $NiCl_2,2{\cdot}5H_2O$, is not known to exist and the other, $CdCl_2,2{\cdot}5H_2O$, which is monoclinic, belongs to a different crystal system.

The ionic radii of cadmium and nickel are 1·03 and 0·78 Å, respectively (Evans, "Crystal Chemistry," Cambridge Univ. Press, 1938), which differ by 32% calculated on the smaller radius. Goldschmidt (*Trans. Faraday Soc.*, 1929, **25**, 253) has shown that isomorphous replacement of atoms does not occur unless the ionic radii differ by less than 15% and their polarisability is about the same, so that in the system $CdCl_2$–$NiCl_2$–H_2O such solid solution is unexpected. When sodium chloride was added to this sytem it was found that it could enter isomorphously into the solid solution $(Cd,Ni)Cl_2,2{\cdot}5H_2O$ replacing the nickel and some of the cadmium. This new solid solution has a wide range of existence starting with the sodium-free $(Cd,Ni)Cl_2,2{\cdot}5H_2O$ and ending with the hexagonal $CdCl_2,2NaCl,3H_2O$. Evidence was brought forward to suggest that solid solution occurs by a replacement of $[Ni(H_2O)_4]^{\cdot\cdot}$ by $[Na_2(H_2O)_2]^{\cdot\cdot}$. A similar solid solution containing sodium chloride was observed in the system $CdCl_2$–$CoCl_2$–H_2O but the sodium-free compound could not be obtained.

The present investigation was undertaken to determine if similar solid solutions with or without sodium chloride occur in other systems containing cadmium chloride and a

* Parts I and II, *J.*, 1939, 646, 653.

bivalent metal chloride. The chlorides investigated were $MgCl_2$, $MnCl_2$, $CuCl_2$, $FeCl_2$ (qualitatively), and $CaCl_2$, chosen for their position in the Periodic Table, their ionic radii, and their different hydrates at 25°. With the exception of the system $CdCl_2$–$FeCl_2$–H_2O these systems have been examined fully at 25° with particular reference to solid solutions, and in all cases sodium chloride was added to the system and a search made for a negative hexagonal phase.

None of the systems dealt with in this paper has been examined previously in detail, though some of the double salts which form congruent solutions had been prepared. Von Hauer recorded $CdCl_2,2MgCl_2,12H_2O$; $2CdCl_2,MnCl_2,12H_2O$; $2CdCl_2,FeCl_2,12H_2O$; $2CdCl_2,CaCl_2,7H_2O$; $CdCl_2,2CaCl_2,12H_2O$, and $CdCl_2,CuCl_2,4H_2O$ (*J. pr. Chem.*, 1856, **68**, 385) and $2CdCl_2,MgCl_2,12H_2O$ (*Sitzungsber. Akad. Wiss. Wien*, 1855, **17**, 331). We have been unable to get the manganese double salt and $2CdCl_2,CaCl_2,7H_2O$ at 25°, though the latter corresponds to the most $CaCl_2$-rich sample of an orthorhombic solid solution represented by ($CdCl_2,H_2O$–$CaCl_2,4H_2O$) obtained by us.

Table 1 shows the double salts and solid solutions we have identified, together with their optical characteristics.

TABLE 1. *Optical properties of solid phases.*

Compound	Crystal habit	Extinction	System	Optical sign
$2CdCl_2,MgCl_2,12H_2O$	Needles with pyramidal ends	All straight	Orthorhombic	Negative
$CdCl_2,2MgCl_2,12H_2O$	Six-sided prisms	Straight or isotropic	Pseudo-hexagonal	Positive
$4CdCl_2,MnCl_2,10H_2O$	Thin needles with poorly formed ends	Straight and a few possibly oblique	Orthorhombic? or monoclinic	Negative
$CdCl_2,CuCl_2,4H_2O$	Thin green needles	Straight and slightly oblique	Monoclinic	Positive
$CdCl_2,2CaCl_2,12H_2O$	Prisms	Straight and oblique	Monoclinic	Negative
Solid solution represented as ($CdCl_2,H_2O$–$CaCl_2,4H_2O$)	Needles	All straight	Orthorhombic	Negative
Metastable solid solution in all systems	Thin hexagonal plates	Isotropic	Hexagonal or pseudo-hexagonal	Negative

The experimental results for the several systems are summarised in Tables 2—11 and shown graphically in Figs. 1—6.

The system $CdCl_2$–$FeCl_2$–H_2O was examined only qualitatively. The solid phases over the whole range of solutions between those saturated with respect to hydrated cadmium chloride and hydrated ferrous chloride were examined under the polarising microscope. Only one new phase was observed, which crystallised in long needles of the negative orthorhombic class. As $2CdCl_2,MgCl_2,12H_2O$ and $2CdCl_2,NiCl_2,12H_2O$ are also negative orthorhombic, it is probable that this new phase is the $2CdCl_2,FeCl_2,12H_2O$ recorded by von Hauer (*loc. cit.*).

EXPERIMENTAL

All solid phases (usually mounted in their own mother-liquor) were examined according to the usual methods with a polarising microscope with rotating stage, before chemical analyses were undertaken (Hartshorne and Stuart, " Crystals and the Polarising Microscope," 1934). Such examination is particularly useful when metastable phases are being investigated, as it can, in most cases, positively confirm that the stable phase is absent, thus guarding against confusing results being obtained by analysing mixtures not in equilibrium with their mother-liquor. Microscopic examination is also invaluable when definite mixtures of two solids are required in order to find an invariant point.

The procedure followed in examining the systems has been previously reported (Bassett, Henshall, Sergeant, and Shipley, *J.*, 1939, 649). As an alternative to the asbestos-coated filter plate in the phase-separation tube previously used, a detachable sintered-glass disc was employed when it was desired to wash crystals free from mother-liquor. A sintered-glass disc 18 mm. in diameter was fitted tightly into a soft rubber ring cut from rubber tubing having a wall thickness of 4—5 mm. : the disc and rubber ring were then wedged into the lower end of the separation tube, which had a slight taper. This assembly was found most reliable and afforded a quick and easy method for the removal of samples for analysis, the disc, rubber ring, and sample being pushed out of the tube by means of a glass rod.

The cadmium chloride used was purified by recrystallisation from water and the other salts were of A.R. quality. The components used in the sodium-free systems were free from sodium.

Analytical Methods.—Total chloride was determined in all cases as a check on the accuracy of the metal determinations. The silver chloride was weighed on a sintered-glass Gooch crucible.

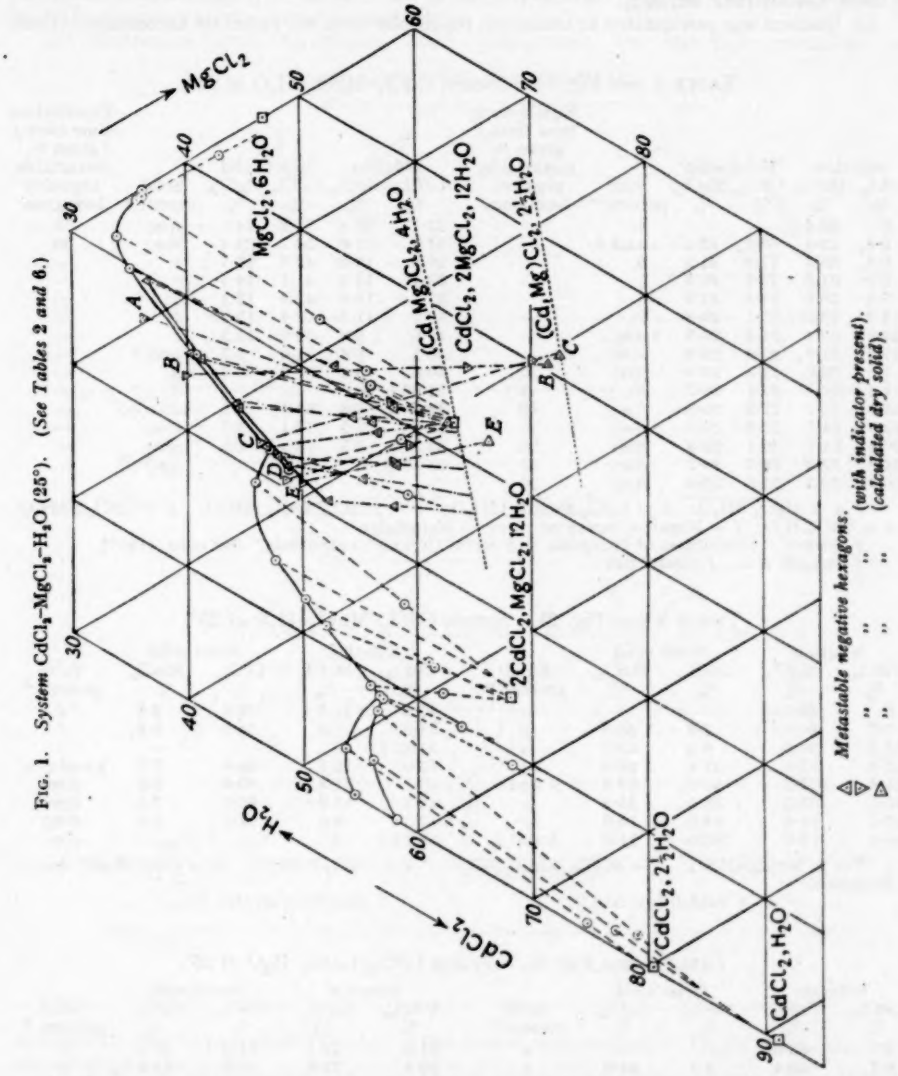


FIG. 1. *System* $CdCl_2$–$MgCl_2$–H_2O (25°). (*See Tables 2 and 6.*)

(i) Cadmium was separated from magnesium or manganese by precipitation as sulphide from weakly acid solution. After being washed with dilute ammonium nitrate saturated with hydrogen sulphide, the precipitate was dissolved immediately in a minimum amount of concentrated hydrochloric acid. The cadmium was then precipitated and weighed as $NH_4CdPO_4.H_2O$ by the procedure described by Bassett *et al.* (*loc. cit.*, p. 650). As the weight of cadmium sulphide recovered from the $NH_4CdPO_4.H_2O$ filtrate varied from 0·1 to 1·0 mg. depending upon the conditions of the experiment, it was normally weighed as such after being washed and dried at 97° on a Gooch crucible. It is known that cadmium is not precipitated as

sulphide of constant composition, but the error introduced is negligible as it only affects a small correction to the main cadmium estimation.

In dealing with cadmium chloride and calcium chloride mixtures, the cadmium was separated by precipitation as the anthranilate, which was weighed after drying at 105° (Funk and Ditt, *Z. anal. Chem.*, 1933, **91**, 332).

(ii) Calcium was precipitated as oxalate in the filtrate from the cadmium anthranilate (Funk

TABLE 2 (see Fig. 1). *System* $CdCl_2$–$MgCl_2$–H_2O *at* 25°.

Solution $CdCl_2$, %	Solution $MgCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $MgCl_2$, %	Solid present *	Equilibrium time (min.) given to metastable negative hexagons	Solution $CdCl_2$, %	Solution $MgCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $MgCl_2$, %	Solid present *	Equilibrium time (min.) given to metastable negative hexagons
0	36·2 †	—	—	*a*	—	27·1	21·8	31·2	24·1	*f*(*m*)	15
0·4$_2$	35·7	0·9$_6$	42·1	*a* and *b*	—	31·4	21·0	34·7	23·4	*f*(*m*)	30
0·4$_3$	35·3	17·5	34·2	*b*	—	26·6	19·2	42·3	16·7	*c*	—
2·3	31·6	23·3	30·4	*b*	—	33·4	14·2	41·1	14·5	*c*	—
5·4	30·0	24·6	31·5	*b*	—	37·7	12·6	47·9	13·1	*c*	—
14·7	26·2	25·1	30·4	*b*	—	40·7	11·5	48·4	13·2	*c*	—
24·9	22·4	34·4	24·8	*b* and *c*	—	47·0	8·9	50·9	11·3	*c*	—
27·2	21·9	29·9	28·8	*b*(*m*)	—	48·1	8·6	54·0	9·7	*c* and *d*	—
7·0	29·6	21·5	29·9	*f*(*m*)	20	50·6	3·2	74·3	0·3$_7$	*d*	—
14·5	26·1	27·1	30·7	*f*(*m*)	5	54·62 ‡	0	—	—	*d*	—
15·1	26·1	27·2	30·8	*f*(*m*)	10	48·5	8·8	59·1	9·2	*c* and *e*(*m*)	—
20·0	24·2	27·6	28·9	*f*(*m*)	20	49·2	7·2	77·1	1·7	*e*(*m*)	—
20·4	24·1	26·1	28·3	*f*(*m*)	25	52·8	3·5	75·9	1·1	*e*(*m*)	—
24·8	22·3	28·5	28·2	*f*(*m*)	35	58·10 ‡	0	—	—	*e*(*m*)	—
26·0	22·3	31·6	26·6	*f*(*m*)	30						

* *a* = $MgCl_2,6H_2O$; *b* = $CdCl_2,2MgCl_2,12H_2O$; *c* = $2CdCl_2,MgCl_2,12H_2O$; *d* = $CdCl_2,2{\cdot}5H_2O$; *e* = $CdCl_2,H_2O$; *f* = Negative hexagons. (*m*) = Metastable.

† Seidell, " Solubilities of Inorganic and Metal Organic Compounds," 3rd edtn. (1940).

‡ Bassett *et al.*, *J.*, 1939, 646.

TABLE 3 (see Fig. 2). *System* $CdCl_2$–$MnCl_2$–H_2O *at* 25°.

Solution $CdCl_2$, %	Solution $MnCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $MnCl_2$, %	Solid present *	Solution $CdCl_2$, %	Solution $MnCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $MnCl_2$, %	Solid present *
0	43·55 †	—	—	*a*	45·5	11·3	73·8	2·3	*c*
7·7	40·4	2·6	55·9	*a*	51·6	2·9	74·3	0·8$_4$	*c*
16·5	36·6	6·8	53·7	*a*	54·62 ‡	0	—	—	*c*
27·5	31·1	37·4	32·9	*a*	43·0	15·3	69·0	7·7	*b* and *d*(*m*)
31·6	27·5	55·9	18·2	*a* and *b*	43·7	14·8	70·6	6·5	*d*(*m*)
36·5	22·2	58·6	15·9	*b*	44·3	13·0	65·0	7·4	*d*(*m*)
37·1	21·9	58·0	15·9	*b*	47·3	8·6	74·3	3·6	*d*(*m*)
40·9	18·0	65·5	11·5	*b* and *c*	58·10 ‡	0	—	—	*d*(*m*)

* *a* = $MnCl_2,4H_2O$; *b* = $4CdCl_2,MnCl_2,10H_2O$; *c* = $CdCl_2,2{\cdot}5H_2O$; *d* = $CdCl_2,H_2O$. (*m*) = Metastable.

† Seidell (*op. cit.*). ‡ Bassett *et al.* (*loc. cit.*).

TABLE 4 (see Fig. 3). *System* $CdCl_2$–$CuCl_2$–H_2O *at* 25°.

Solution $CdCl_2$, %	Solution $CuCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $CuCl_2$, %	Solid present *	Solution $CdCl_2$, %	Solution $CuCl_2$, %	Moist solid $CdCl_2$, %	Moist solid $CuCl_2$, %	Solid present *
0	43·6	—	—	*a*	31·8	25·1	41·8	31·0	*b*
8·2	39·4	4·2	64·0	*a*	36·4	22·6	42·6	28·3	*b*
13·7	36·8	4·5	68·2	*a*	38·8	21·1	60·8	15·7	*b* and *d*
21·4	32·4	11·9	53·9	*a*	39·7	18·8	75·7	5·4	*c* and *d*
22·4	32·0	28·1	45·3	*a* and *b*	47·4	7·1	75·9	1·0	*c*
23·7	31·4	38·6	33·0	*b*	54·62 †	0	—	—	*c*
24·4	30·7	38·4	32·8	*b*	38·6	20·6	69·6	8·8	*d*(*m*)
28·1	27·6	40·0	32·1	*b*	46·5	11·0	71·2	4·0	*d*(*m*)
30·5	26·2	38·3	30·3	*b*	53·5	4·3	80·3	1·6	*d*(*m*)
30·7	26·4	41·0	31·3	*b*	58·10 †	0	—	—	*d*(*m*)

* *a* = $CuCl_2,2H_2O$; *b* = $CdCl_2,CuCl_2,4H_2O$; *c* = $CdCl_2,2{\cdot}5H_2O$; *d* = $CdCl_2,H_2O$. (*m*) = Metastable.

† Bassett *et al.* (*loc. cit.*).

and Ditt, *loc. cit.*), and, after being washed with a saturated solution of calcium oxalate (Bassett, *J.*, 1934, 1273), it was determined volumetrically with 0·1N-potassium permanganate.

(iii) Copper was precipitated and weighed as cuprous thiocyanate in the presence of sulphur dioxide. The ammonium thiocyanate in the filtrate from the latter does not intefere with the precipitation and weighing of the cadmium as $NH_4CdPO_4.H_2O$. Sulphur dioxide was removed by boiling before precipitation of the cadmium.

(iv) Magnesium and manganese were precipitated by standard procedure as

FIG. 2. *System* $CdCl_2$–$MnCl_2$–H_2O (25°).

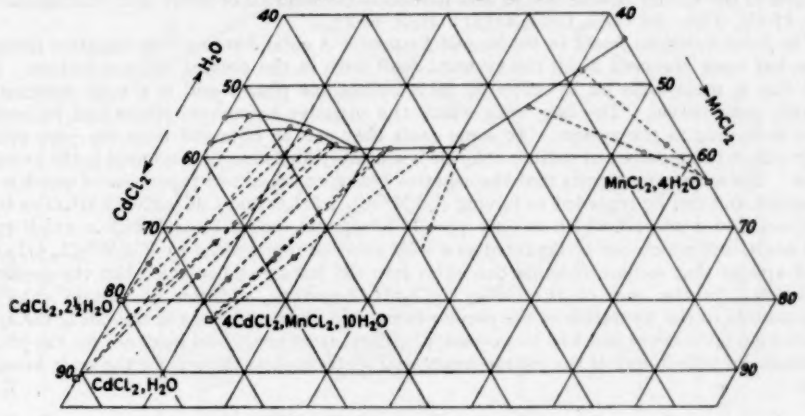
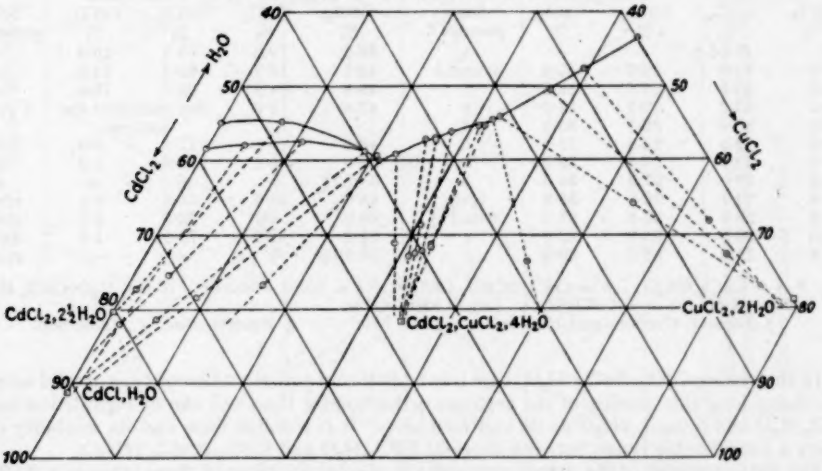


FIG. 3. *System* $CdCl_2$–$CuCl_2$–H_2O (25°).



$NH_4MgPO_4.xH_2O$ and $NH_4MnPO_4.H_2O$. The former was weighed as $Mg_2P_2O_7$, and the latter was weighed as such.

(v) Sodium was precipitated as $NaZn(UO_2)_3(C_2H_3O)_9.6H_2O$ in the presence of the other metals and weighed as such, standard procedure being followed.

(vi) Bromate was determined iodometrically by Kolthoff's method (*Pharm. Weekblad*, 1919, **56**, 393) in acid solution, ammonium molybdate being used as catalyst.

Since the two double salts $CdCl_2.2MgCl_2.12H_2O$ and $2CdCl.MgCl_2.12H_2O$ form congruent solutions, the methods of preparation given by von Hauer (*loc. cit.*) are satisfactory.

The one double salt, namely, $4CdCl_2.MnCl_2.10H_2O$, does not form a congruent solution. The double salt $2CdCl_2.MnCl_2.12H_2O$ reported by von Hauer could not be obtained at 25° even after

seeding with the corresponding cadmium magnesium double salt, nor was there any indication from optical examinations that this double salt exists at higher temperatures. Its existence is clearly open to doubt.

The tie lines in Fig. 3 scarcely enable a clear decision to be made as to whether the double salt has three or four molecules of water of crystallisation. As the salt forms a congruent solution, the matter could be settled by analysis of the crystals obtained at 25° from a solution containing the constitutent salts in exact equimolar proportion. The crystals were well dried between hardened filter-paper and air-dried at room temperature, reaching constant weight after 24 hours. Analysis of the air-dry double salt to give indirectly the amount of water of crystallisation gave H_2O, 17·8% (Calc. for $CdCl_2,CuCl_2,4H_2O$: H_2O, 18·2%).

The Solid Solutions found in the Several Systems.—A solid forming thin negative hexagonal plates has been observed in all the systems dealt with in the present communication. In all cases this is metastable at 25° towards other crystalline phases and is a solid solution with variable composition. The ease with which the negative hexagonal plates can be obtained varies according to the system. In some cases they can be obtained from the pure systems, but in others the presence of sodium chloride is necessary and some of it is found in the hexagonal plates. The evidence suggests that the negative hexagons are of two types, one of which is truly hexagonal and can be regarded as having $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$ and $CdCl_2,2NaCl,3H_2O$ as its end members, and a second which is only pseudo-hexagonal, being biaxial with a small optical axial angle, and which can be regarded as a solid solution represented by $(Cd,M^{II})Cl_2,4H_2O$. It would appear that sodium chloride can enter into the latter solid solution but the evidence is conflicting. In the case of the $CdCl_2$–$MgCl_2$–H_2O system, addition of sodium chloride is unfavourable to the formation of the pseudo-hexagonal plates, whereas in the $CdCl_2$–$CaCl_2$–H_2O system such addition appears to be necessary. There is no analytical evidence for the presence of sodium chloride in any of the pseudo-hexagonal plates such as there is for the truly hexagonal forms.

TABLE 5 (see Fig. 4). *System* $CdCl_2$–$CaCl_2$–H_2O *at* 25°.

Solution		Moist solid			Solution		Moist solid		
$CdCl_2$, %	$CaCl_2$, %	$CdCl_2$, %	$CaCl_2$, %	Solid present *	$CdCl_2$, %	$CaCl_2$, %	$CdCl_2$, %	$CaCl_2$, %	Solid present *
0	45·05 †	—	—	*a*	38·3	19·3	57·7	19·2	*c*
1·6	44·6	6·6	47·4	*a* and *b*	43·1	16·7	61·1	14·5	*c*
4·5	39·8	24·6	36·9	*b*	46·8	14·9	62·2	10·9	*c*
8·7	37·5	27·3	35·7	*b*	47·8	11·3	Not sufficient for analysis		*d* and *e*
12·0	35·0	26·1	36·5	*b*					
16·5	32·5	28·6	35·2	*b*	48·6	8·3	77·7	0·8$_7$	*d*
17·8	32·2	27·9	36·0	*b*	50·0	6·1	73·0	1·3	*d*
21·8	30·5	27·9	34·5	*b*	54·62 ‡	0	—	—	*d*
24·8	29·1	28·6	35·3	*b*(*m*)	48·6	10·0	72·6	4·1	*e*(*m*)
24·3	28·8	39·4	27·2	*b* and *c*	48·9	8·9	72·5	4·4	*e*(*m*)
25·0	28·3	55·3	22·2	*c*	51·8	5·6	78·1	1·5	*e*(*m*)
32·8	21·7	51·3	20·9	*c*	58·10 ‡	0	—	—	*e*(*m*)

* *a* = $CaCl_2,6H_2O$; *b* = $CdCl_2,2CaCl_2,12H_2O$; *c* = Solid solution ($CdCl_2,H_2O$–$CaCl_2,4H_2O$); *d* = $CdCl_2,2{\cdot}5H_2O$; *e* = $CdCl_2,H_2O$. (*m*) = Metastable.

† Bassett, Gordon, and Henshall, *J.*, 1937, 971. ‡ Bassett *et al.*, *J.*, 1939, 646.

In the system $CdCl_2$–$CaCl_2$–H_2O there is in addition an entirely different type of solid solution. This forms long thin needles of the negative orthorhombic class and can be regarded as having $CdCl_2,H_2O$ and β-$CaCl_2,4H_2O$ as its end members. It is a stable form and its solubility curve covers a considerable range between those of $CdCl_2,H_2O$ and $CdCl_2,2CaCl_2,12H_2O$.

The determination of the actual composition of solid solutions of these types is a matter of extreme difficulty. In some cases we have removed adhering mother-liquor from the crystals by means of organic solvents; in other cases we have added suitable substances in small amounts to the system which would enable the composition of the dry solid, free from mother-liquor, to be calculated. The results obtained are considered to be reasonably reliable. The experimental results are shown in Tables 6—11 and Figs. 1, 4, 5, and 6. The double salt $2CdCl_2,CaCl_2,7H_2O$ recorded by von Hauer (*loc. cit.*) would have a calculated composition of $CdCl_2$, 60·7% and $CaCl_2$, 18·4%. This corresponds to the composition found for the most $CaCl_2$-rich sample of this solid solution (see Fig. 4) and would be expected from the ratio of salts used by von Hauer ($CdCl_2 : CaCl_2 = 4 : 3$).

The theoretical explanation of these peculiar solid solutions must clearly pay great attention

to the best-defined case of all, namely, that found in the systems $CdCl_2$–$NiCl_2$–H_2O and $CdCl_2$–$NiCl_2$–NaCl–H_2O (Bassett *et al.*, *loc. cit.*). The suggestion made there was that the process involved was a gradual replacement of $[Ni(H_2O)_4]^{\cdot\cdot}$ or $[Cd(H_2O)_4]^{\cdot\cdot}$ by $[Na_2(H_2O)_4]^{\cdot\cdot}$.

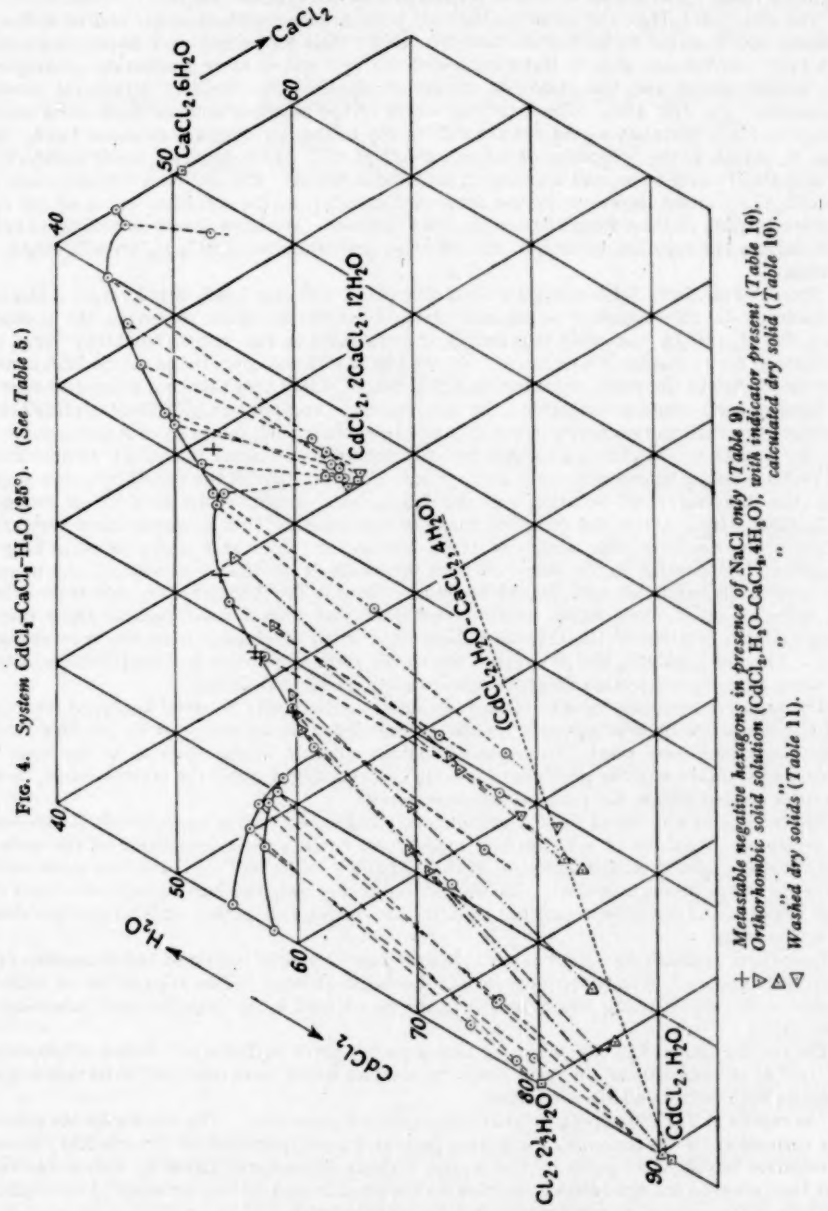


FIG. 4. *System* $CdCl_2$–$CaCl_2$–H_2O (25°). (*See Table* 8.)

It is perhaps more probable that a layer-lattice structure is built up with layers of $CdCl_2,2NaCl,3H_2O$ and layers of $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$. It is quite possible that the structure of $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$ and $CdCl_2,2NaCl,3H_2O$ might be sufficiently similar for the formation of

layer-lattice intergrowths. The additional stability introduced by the $CdCl_2,2NaCl,3H_2O$ might enable a hexagonal form of $(Cd,M^{II})Cl_2,2{\cdot}5H_2O$ to occur which is not capable of existing in the free state. In a similar way the pseudo-hexagonal compound when it contains sodium might be made up of layers of $(Cd,M^{II})Cl_2,4H_2O$ and $CdCl_2,2NaCl,3H_2O$.

The salts $CdCl_2,H_2O$ and β-$CaCl_2,4H_2O$ are both negative orthorhombic and so is the solid solution which seems to be formed between them; this too might well have a layer-lattice structure. Structures akin to those suggested are well known among minerals—examples are the humite group and the staurolite group of silicates (see Wells, " Structural Inorganic Chemistry," pp. 470, 472). The solubility curve of the negative orthorhombic solid solution, were it not too unstable, would cut the side of the triangular diagram at about $CaCl_2$, 51·3% (Fig. 4), which is the solubility of β-$CaCl_2,4H_2O$ at 25°. This confirms other evidence that β-$CaCl_2,4H_2O$ could be an end member of the solid solution. The ordinary orthorhombic form of $CdCl_2,H_2O$ cannot, however, be the other end member, as the solubility curve of the monohydrate is quite distinct from that of the solid solution. We have observed nothing to suggest that sodium chloride can enter into the negative orthorhombic ($CdCl_2,H_2O$–$CaCl_2,4H_2O$) solid solution.

Details of the Solid Solutions in the Several Systems.—System $CdCl_2$–$MgCl_2$–H_2O. The forms crystallising in thin negative hexagonal plates exist in the same region as the compound $CdCl_2,2MgCl_2,12H_2O$, and since it is only just metastable to this salt its solubility curve could be followed for a considerable distance. At the $MgCl_2$-rich end of its range the tie lines converge very closely on to the point representing $CdCl_2,2MgCl_2,12H_2O$, so this would seem to represent the limit of solid-solution formation. In this region the compound $CdCl_2,2MgCl_2,12H_2O$ can be considered to exist in two polymorphic forms. In contact with solutions containing more than 25% by weight of $CdCl_2$ the solid phase becomes progressively richer in this salt as indicated by the tie lines failing to converge on a single point. The position of the solubility curve suggests that the limiting solid solution on the $CdCl_2$ side might correspond to a compound $CdCl_2,MgCl_2,8H_2O$. Over the complete range of existence the thin hexagons have very similar optical properties with edge angles of 120°, the face of the crystal plates showing long thin troughs etched parallel to the sides. Under favourable crystallising conditions the hexagons can have a thicker habit and display secondary faces. The hexagons are not truly uniaxial but show an interference figure which becomes biaxial with a small optical angle (pseudo-hexagonal) on rotation of the crystal, indicating a small divergence from the true hexagonal form. The $CdCl_2,2MgCl_2,12H_2O$ crystals are in the form of positive hexagonal columns which can show a hexagonal section which is also optically pseudo-hexagonal.

The negative hexagons were too thin to be dried mechanically between hardened filter-paper and too soluble in organic solvents for the mother-liquor to be removed by washing, though various mixtures were tried. Addition of sodium chloride to the system, in the hope that increase in stability and the presence of sodium chloride might make the crystals easier to wash free from mother-liquor, led to no satisfactory results.

Sulphuric acid was found to be a satisfactory " indicator " when added in small amounts to the mixtures. Analysis of solution and moist solid enables the composition of the pure dry solid to be calculated on the assumption that all the " indicator " found in the moist solid is present in the adhering solution. The metastable phase normally had an existence time of up to 30 minutes and could be separated by filtration during this period without precipitation of the stable phase.

Potassium bromate was tried as an indicator but it greatly increased the instabilty of the negative hexagons; even when only 5 minutes were allowed before separation of solid and solution, some stable phase was observed in the moist solid a few minutes after sampling had taken place.

The results obtained by the indicator technique are given in Table 6. Where sulphuric acid was used as an indicator all the results refer to samples which were observed to be thin negative hexagons both before and after filtration.

The results in Table 6 appear to be of considerable significance. The results for the solutions after correction for the amount of indicator present do not quite fall on the solubility curve of the negative hexagons as given by the results without indicator in Table 2; this is due to the short time allowed for equilibrium and the disturbance caused by the presence of the indicator especially when present in comparatively high concentration.

Experiment *A* gives a result for the dry solid which agrees exactly with the indications given by the convergence of the tie lines in that region of the diagram. This shows that the indicator method using sulphuric acid can be regarded as giving reliable results.

Experiment *E* gives a point falling close to, though somewhat below the line $(Cd,Mg)Cl_2,4H_2O$, but though it indicates an increase in the proportion of $CdCl_2$ relatively to that of $MgCl_2$ it cannot be regarded with much confidence for the reason mentioned above.

Experiments *B* and *C* give results which are especially interesting as they both give points for the dry solid lying almost exactly on the $(Cd,Mg)Cl_2,2{\cdot}5H_2O$ line. Both are close to the position represented by $2CdCl_2,5MgCl_2,17{\cdot}5H_2O$ (Calc.: $CdCl_2$, 31·7; $MgCl_2$, 41·2%). This

TABLE 6 (see Fig. 1). *Composition of* $CdCl_2,MgCl_2$ *negative hexagons* (25°).

Equilibrium time (min.)	Solution *				Moist solid *				Calculated dry solid		Ref. in Fig. 1
	$CdCl_2$, %	$MgCl_2$, %	H_2SO_4, %	$KBrO_3$, %	$CdCl_2$, %	$MgCl_2$, %	H_2SO_4, %	$KBrO_3$, %	$CdCl_2$, %	$MgCl_2$, %	
	(9·7)	(26·9)			(27·0)	(31·0)					
25	9·6	26·7	$0{\cdot}6_5$	—	26·9	31·0	$0{\cdot}1_4$	—	31·9	32·2	*A*
	(15·7)	(24·1)			(27·6)	(37·0)					
30	14·7	22·6	$6{\cdot}1_5$	—	27·2	36·5	$1{\cdot}3_4$	—	30·7	40·5	*B*
	(24·1)	(22·6)			(29·9)	(40·2)					
30	24·0	22·5	$0{\cdot}3_5$	—	29·9	40·2	0·03	—	30·5	42·0	*C*
20	27·8	21·0	†	—	31·7	28·9	†	—	—	—	*D*
	(29·1)	(21·4)			(31·5)	(26·8)					
5	28·8	21·1	—	1·13	31·3	26·7	—	0·57	33·9	32·4	*E*

* Figures in parentheses are calculated by neglecting amount of " indicator " present.
† Small amount, not determined.

seems to show that the metastable hexagons found in the system $CdCl_2$–$MgCl_2$–H_2O are of two types: (*a*) biaxial (pseudo-hexagonal) solid solution—$(Cd,Mg)Cl_2,4H_2O$; (*b*) uniaxial, hexagonal, solid solution—$(Cd,Mg)Cl_2,2{\cdot}5H_2O$. Type (*a*) appears to be more stable and more readily obtained than type (*b*).

It must be remembered that the tie lines relating to solid solutions are liable to be somewhat erratic, owing to the fact that, although the surface layers of the solid phase are in equilibrium with the solution, the composition will change with growth. The gross composition of the solid phase will therefore vary somewhat according to the relative proportions of the solid phase which have separated in different experiments. Poggiale (*Compt. rend.*, 1870, **70**, 1130) records a compound $MgCl_2,NaCl,2H_2O$, but Keitel (*Kali*, 1923, **17**, 248, 261) could not confirm this and says that $MgCl_2$ and NaCl form no double salts or solid solutions.

System $CdCl_2$–$MnCl_2$–NaCl–H_2O. No negative hexagons were obtained in the system $CdCl_2$–$MnCl_2$–H_2O but in the presence of sodium chloride they appeared. With a molecular ratio $MnCl_2 : CdCl_2 = 2{\cdot}2 : 1$ they could not be obtained if the NaCl content was less than 0·5% (calculated on the total anhydrous salts). As the proportion of NaCl was increased to 15%, the stability of the hexagons was found to increase. Their appearance was identical with that of hexagons found in the $CdCl_2$–$MgCl_2$–H_2O system but, unlike the latter, they always gave a true uniaxial interference figure.

The negative hexagons were too thin for mechanical drying, and although various substances were tried as indicators none was found suitable. The presence of sulphate caused the hexagons to become very unstable, whereas bromate caused oxidation trouble, and so on. A satisfactory washing technique was, however, developed which enabled a dry preparation to be obtained for analysis. Acetone or acetone–ether caused precipitation from the mother-liquor but it was found that a slightly warmed mixture of 90% acetone and 10% water (by vol.) was satisfactory as a first wash liquid and the following procedure gave crystals of the negative hexagons uncontaminated by the component salts or $4CdCl_2,MnCl_2,10H_2O$: the moist crystals were sucked as dry as possible on a sintered-glass crucible, then washed successively 3 times with the above warm mixture of acetone and water, 3 times with acetone, and twice with ether (dried over sodium), and finlly kept at room temperature for 15 minutes before sampling for analysis. Owing to the tendency of the thin plates to pack tightly under suction, only small quantities of the solid could be satisfactorily washed at one time.

The composition of a number of preparations of the dry negative hexagons separated in the above manner is given in Table 7 and shown graphically in Fig. 5.

It must be admitted that, whatever the care used, separation of solid from aqueous phases by washing with organic solvents is always subject to some uncertainty. The points for the solid solutions in Fig. 5 fall at some distance from the line joining the points $CdCl_2,2NaCl,3H_2O$ and $(Cd,Mn)Cl_2,2{\cdot}5H_2O$. However, as the results obtained in the $CdCl_2$–$NiCl_2$–NaCl–H_2O system

were much more definite because the negative hexagons were obtainable as much larger crystals, it is reasonable to conclude that, since the negative hexagons in both systems are optically completely similar, the manganese crystals are solid solutions between $(Cd,Mn)Cl_2,2{\cdot}5H_2O$ and

TABLE 7 (see Fig. 5). *System* $CdCl_2$–$MnCl_2$–NaCl–H_2O (25°) : *negative hexagons.*

Composition, % (by wt.)			Composition, % (molar)			Composition, % (by wt.)			Composition, % (molar)		
$CdCl_2$	$MnCl_2$	NaCl	$CdCl_2$	$MnCl_2$	NaCl	$CdCl_2$	$MnCl_2$	NaCl	$CdCl_2$	$MnCl_2$	NaCl
55·9	12·4	8·0	16·4	5·3	7·4	60·1	2·5	22·7	21·1	1·3	25·0
54·8	15·0	7·7	16·7	6·7	7·4	56·8	1·0	28·6	19·8	0·5	31·2
55·7	13·6	9·5	17·4	6·2	9·3	55·6	2·6	28·8	19·7	1·4	32·1

$CdCl_2,2NaCl,3H_2O$. The system $MnCl_2$–NaCl–H_2O was examined qualitatively by observing the optical properties of the solid phases and no indication was obtained for the existence of any double salt.

System $CdCl_2$–$CuCl_2$–H_2O. No negative hexagons were observed in this system in the absence of sodium chloride, but on addition of the latter small plates of this nature were obtained when the molecular ratio $CdCl_2 : CuCl_2$ ranged from 0·35 to 0·96. These plates, which were pseudo-hexagonal, were very unstable and were always observed in the presence of the stable phase. No detailed study of their chemical composition was possible.

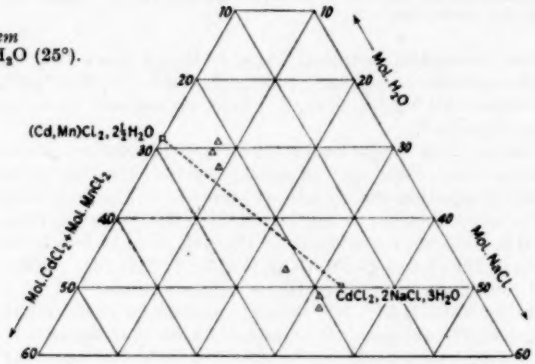


FIG. 5. *System* $CdCl_2$–$MnCl_2$–NaCl–H_2O (25°).

No double salts have been observed in the system $CuCl_2$–NaCl–H_2O at 30° (Schreinemakers and de Baat, *Z. physikal. Chem.*, 1909, **65**, 586).

System $CdCl_2$–$FeCl_2$–H_2O. In this system also the hexagons could only be obtained in the presence of sodium chloride and were observed when the molecular ratio $CdCl_2 : FeCl_2$ varied from 0·9 to 1·7. They were very unstable, were usually contaminated with the stable phase, and were not examined further.

System $CdCl_2$–$CaCl_2$–H_2O. When sodium chloride is added to this system, and in its presence only, a new phase occurs, crystallising in thin plates, which is metastable to the orthorhombic solid solution ($CdCl_2,H_2O$–$CaCl_2,4H_2O$). Under favourable conditions the plates can have a regular hexagonal outline, but this is generally irregular. The crystals are negative hexagonal but have been observed in a few instances to give a uniaxial interference figure in white light which becomes biaxial on rotation, so that in such cases the crystals are only pseudo-hexagonal. This is like the case of the negative hexagons in the system $CdCl_2$–$MgCl_2$–NaCl–H_2O and may mean that there are two types of negative hexagonal phase—one uniaxial and truly hexagonal which is a layer lattice structure built up from $(Cd,Ca)Cl_2,2{\cdot}5H_2O$ and $CdCl_2,2NaCl,3H_2O$, and a second, biaxial and pseudo-hexagonal which is the solid solution $(Cd,Ca)Cl_2,4H_2O$. It was found that the negative hexagons occurred over the range where the molecular ratio $CdCl_2 : CaCl_2$ was 0·5 to 1·8 provided that the NaCl content was from 2 to 10% of the total weight of the mixture. These were the most stable and easiest to handle of all the metastable hexagons observed in the present investigation.

Two series of preparations of the negative hexagons were separated in the dry condition by washing with mother-liquor–alcohol mixtures of increasing alcohol content and then with

alcohol–ether mixtures of increasing ether content. The washed crystals were then air-dried. The compositions of one series are given in Table 8.

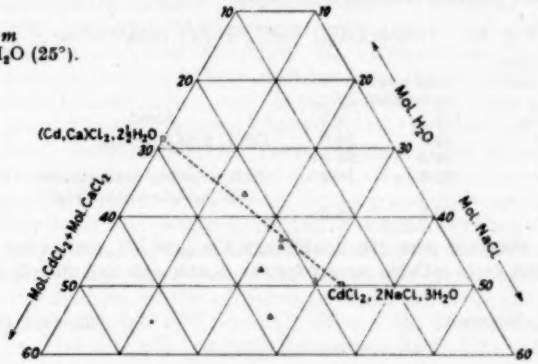
TABLE 8 (see Fig. 6). *System* $CdCl_2$–$CaCl_2$–NaCl–H_2O (25°) : *negative hexagons.*

(Mol. ratio $CdCl_2 : CaCl_2 = 1{\cdot}33$.)

Concn. of NaCl in (mixture (%)	Composition of washed dry solid, % By analysis			Calculated molecular proportions			
	$CdCl_2$	$CaCl_2$	NaCl	$CdCl_2$	$CaCl_2$	NaCl	H_2O
2	61·7	4·8	14·1	19·8	2·6	14·2	63·4
2½	59·5	2·4	21·3	19·7	1·3	22·2	56·8
3	60·4	2·2	21·3	20·5	1·2	22·7	55·6
4	54·2	2·8	28·1	18·2	1·6	29·6	50·6

These results are shown in Fig. 6 and can certainly be regarded as showing that the negative hexagons were solid solutions covering the range $(Cd,Ca)Cl_2,2{\cdot}5H_2O$ to $CdCl_2,2NaCl,3H_2O$. The agreement is as good as can be expected from the method.

FIG. 6. *System* $CdCl_2$–$CaCl_2$–NaCl–H_2O (25°).



The results of another series examined earlier are shown in Table 9.

TABLE 9 (see Figs. 4 and 6). *System* $CdCl_2$–$CaCl_2$–NaCl–H_2O (25°) : *negative hexagons.*

(Sodium chloride concentration constant at 2%.)

Mol. ratio $CdCl_2$/$CaCl_2$	Liquid, %			Moist solid, %			Washed dry solid: By analysis, %			Washed dry solid: Mol. proportions, % (calc.)			
	$CdCl_2$	$CaCl_2$	NaCl	$CdCl_2$	$CaCl_2$	NaCl	$CdCl_2$	$CaCl_2$	NaCl	$CdCl_2$	$CaCl_2$	NaCl	H_2O
0·48	21·1	32·0	0·4	—	—	—	—	—	—	—	—	—	—
0·61	30·5	23·0	0·7	46·4	18·1	7·0	57·7	8·9	21·8	22·3	5·7	26·4	45·6
1·33	37·6	19·2	1·0	—	—	—	—	—	—	—	—	—	—
1·33	38·3	19·0	1·0	51·3	13·7	6·9	61·7	4·8	14·1	19·8	2·6	14·2	63·4
1·82	43·6	16·3	0·9	53·5	12·8	6·4	61·7	5·4	18·9	22·6	3·2	21·7	52·4

These results are useful because, owing to the small percentage of NaCl in the solution, this salt can be treated as an inert constituent and plotted in Fig. 4 to show the approximate relationship which the metastable negative hexagonal solid solution $(Cd,Ca)Cl_2,2{\cdot}5H_2O$ would have to the other solid phases if realisable in the absence of sodium chloride. The data for the three dry solid phases are plotted in Fig. 6. The compositions of two of the solids only appear explicable on the assumption that appreciable contamination of the metastable negative hexagons had occurred. Contamination with the stable phase ($CdCl_2,H_2O$–$CaCl_2,4H_2O$) which can have about 1—2 mols. of H_2O per mol. of $(Cd,Ca)Cl_2$ would not alone produce these results, but the anhydrous bivalent salts would, and although these were not detected optically, much practical difficulty had been experienced with these particular experiments.

Two methods have been used for determining the composition of the negative orthorhombic solid solution. At the $CdCl_2$-rich end of the series, the indicator method with potassium bromate was found to be satisfactory. The results seem to show definitely that the solid solution is between some form of $CaCl_2,4H_2O$ (possibly the β-form) and $CdCl_2,H_2O$. The presence of the

indicator ($KBrO_3$) is bound to cause some disturbance of the equilibrium conditions between the solid and liquid. Probably for this reason the solution points of the bromate experiments do not always fall quite on the solubility curve of the solid solutions, while the solution–moist solid tie-lines slope at a different angle from those in the absence of bromate.

TABLE 10 (see Fig. 4). *Negative orthorhombic solid solution* ($KBrO_3$ *indicator method*).

Liquid, %			Moist solid, %			Dry solid composition, % (calc.)	
$CdCl_2$	$CaCl_2$	$KBrO_3$	$CdCl_2$	$CaCl_2$	$KBrO_3$	$CdCl_2$	$CaCl_2$
29·8	25·0	0·171	53·1	19·8	0·059	65·3	17·1
36·5	21·7	0·137	54·6	19·0	0·055	66·9	17·2
42·0	17·9	0·124	55·1	14·4	0·076	75·6	9·0
45·0	15·4	0·258	60·4	10·7	0·127	80·3	6·1
43·8	16·4	0·136	58·1	11·2	0·094	90·3	Nil or very small

In the $CaCl_2$-rich region of ($CdCl_2,H_2O$–$CaCl_2,4H_2O$) and for $CdCl_2,2CaCl_2,12H_2O$ the crystals could be obtained free from mother-liquor by the washing technique already described for the negative hexagons. Table 11 shows several results obtained in this manner and also one for crystals dried by hand pressure between filter-paper.

TABLE 11 (see Fig. 4). *System* $CdCl_2$–$CaCl_2$–H_2O : *composition of washed dry solid.*

Estimated approximate composition of mother-liquor, %		Composition of washed solid, %			
$CdCl_2$	$CaCl_2$	$CdCl_2$	$CaCl_2$	Solid	Washing technique
16	33	29·0	36·6	$CdCl_2,2CaCl_2,12H_2O$	EtOH–mother-liquor
22	30	29·5	34·9	,,	,, ,,
29	24	62·6	19·2	Orthorhombic solid solution ($CdCl_2,H_2O$–$CaCl_2,4H_2O$)	EtOH–Et_2O ,,
33	22	60·1	18·5	,, ,,	Hand-dried

The two results obtained with the double salt $CdCl_2,2CaCl_2,12H_2O$ are important as they show that the method gives reliable results for the double salt and should do the same for the solid solutions.

THE UNIVERSITY, READING. [*Received, December 1st*, 1951.]

332. *Sorption Hysteresis. Part II.* The Rôle of the Cylindrical Meniscus Effect.*

By A. GRAHAM FOSTER.

The correct formulation of the equations for the cylindrical meniscus effect is discussed and applied to a critical review of Cohan's theory of the point of hysteresis inception. It is shown that during the early stages of the sorption process the effect assists layer formation and that Cohan's mechanism for pore blocking becomes operative later, only if certain conditions are fulfilled. The potential due to layer adsorption is calculated from Brunauer, Emmett, and Teller's (B.E.T.) theory and compared with that due to capillary condensation in the same pore. The total potential, arising from the combination of layer adsorption with the cylindrical meniscus effect, passes through a minimum at some stage of the sorption process and it is suggested that hysteresis will occur only when the Kelvin potential curve intersects this total potential curve before the minimum is reached. When both the pore radius and the number of adsorbed layers are large, a simplified mathematical treatment leads to the prediction that hysteresis is possible when the product $V\gamma/RT\sigma$ for the adsorbed liquid exceeds unity (where V is the molar volume, γ the surface tension, and σ the molecular diameter).

THE open-pore theory of sorption hysteresis (Foster, *Trans. Faraday Soc.*, 1932, **28**, 645) assumes that the equilibrium pressures on the desorption branch of the hysteresis loop are determined by the Kelvin equation, and attributes the higher pressures observed during adsorption to delayed meniscus formation. The adsorptive forces become weaker

* Part I, *J. Phys. Colloid. Chem.*, 1951, **55**, 638.

as layer formation proceeds and molecules are held at a greater distance from the surface. At the same time, the space remaining empty in the centre of the capillaries becomes smaller and a point is reached at which the cohesive forces should, by capillary condensation, be able to effect a greater lowering of vapour pressure than the adsorptive forces. It is, however, not possible for condensation to occur at this stage unless the pores are already blocked at their narrowest points by the adsorbed layer. If no meniscus is present the liquid must remain on the walls until a higher pressure is reached. In its original form the open-pore theory assumed that layer adsorption persisted until enough liquid was present to block the pores and form a meniscus. It was later pointed out (Foster, *Proc. Roy. Soc.*, 1934, *A*, **147**, 138) that continued layer adsorption would be assisted by a capillary condensation effect, due to the cylindrical meniscus presented by the adsorbed layer, which produces a free-energy decrease approximately one-half of that due to normal condensation at a spherical meniscus in a pore of the same radius. An analysis of the extensive data of Lambert and Clark (*ibid.*, 1929, *A*, **122**, 497) for the sorption of benzene by ferric oxide gel showed that the desorption equilibria were consistent with the capillary theory, whilst the adsorption equilibria were consistent with the Polanyi "potential" theory (*Verhandl. deut. physik. Ges.*, 1916, **18**, 55) of multimolecular adsorption. Later Brunauer, Deming, Deming, and Teller (*J. Amer. Chem. Soc.*, 1940, **62**, 1723) showed that these adsorption data could be interpreted satisfactorily by a modification of the original B.E.T. theory.

In Cohan's version (*J. Amer. Chem. Soc.*, 1944, **66**, 98) of the open-pore theory, multilayer formation is ignored and all sorption effects beyond the monolayer are attributed to capillary condensation. During adsorption, the equilibria are determined by the cylindrical meniscus effect, and during desorption by the normal condensation process in accordance with the Kelvin equation. Both branches of the loop are thus attributed to capillary effects, and the theory leads to a simple quantitative relation between the adsorption and desorption pressures in pores of given radius. It is further predicted that the pressure at which hysteresis begins (point of hysteresis inception) should correspond to a Kelvin radius $r = 2\sigma$, where σ is the diameter of the adsorbed molecule (or, more strictly, the thickness of an adsorbed layer). Emmett and Cines (*J. Phys. Coll. Chem.*, 1947, **51**, 1260) have pointed out that the observed radii generally lie between 2σ and 3σ and have predicted a value of 3σ, a slight modification of Cohan's original argument being used. Some recent observations (Brown and Foster, *J. Phys. Coll. Chem.*, in the press) on the sorption of amines by silica gels also indicate values lying between 2σ and 3σ.

Cohan used an approximate equation for the cylindrical meniscus effect which is not accurate for small radii, and the original object of this paper was to repeat his calculations, using the correct equation. This led to the view that a value 3σ for the radius at the point of hysteresis inception could be predicted by assuming more extensive layer formation during adsorption than during desorption—a view which, although quite plausible, is untenable in a theory which postulates that layer adsorption does not extend beyond the monolayer. In attempting to develop a more consistent theory, the basic ideas of the author's original version have been combined with Cohan's idea that the cylindrical meniscus effect provides a mechanism for pore filling. The following discussion thus falls into three parts: (*a*) a correct formulation of the equations for the cylindrical meniscus effect, (*b*) a critical review of Cohan's theory of the point of hysteresis inception, and (*c*) an attempt to combine the basic ideas of the two versions of the "open-pore" theory.

Theory of the Cylindrical Meniscus Effect.—According to the Kelvin equation the vapour pressure of a liquid of surface tension γ and molar volume V contained in a cylinder of radius r is given by

$$p = p_0 \exp(-2V\gamma/rRT) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where p_0 is the saturation vapour pressure over a plane surface at the same temperature T. Since there must be an adsorbed layer present on the walls of the pore before condensation can occur, r is not the true pore radius r_0 but is lower by an amount D which represents the thickness of this layer. It is generally assumed that the vapour pressure over a cylindrical meniscus is given by

$$p = p_0 \exp(-V\gamma/rRT) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

since the Gauss curvature of the cylindrical surface is half that of the corresponding spherical surface. However, this is no longer quite true when r is of the same order as the molecular diameter σ. The correct relation (Foster, *loc. cit.*, 1934) is

$$p = p_0 \exp\{-V\gamma/(r - \sigma/2)RT\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

which reduces to (2) when $r \gg \sigma$. An alternative form of this equation, which will be used later, is

$$p = p_0 \exp\{-V\gamma/(r + \sigma/2)RT\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3a)$$

where r is taken as the *final* radius, the *initial* radius being $r + \sigma$.

Point of Hysteresis Inception.—The essential feature of Cohan's theory is that when the pressure, during adsorption, reaches a value p_a given by equation (2), the capillary fills completely, whereas during desorption the same pore will not empty until the pressure has been reduced to the lower value p_d given by equation (1). The reason for complete filling at p_a is that, although initially the pressure must by raised to this value in order that one more layer may condense on the walls, yet once this layer has formed, a second can then form at the still lower pressure corresponding to $r - \sigma$, and so on until the pore is completely filled. Cohan assumes that the mechanism of adsorption on a porous solid consists in the formation of a unimolecular layer followed by capillary condensation, but in applying the Kelvin equation he takes the radius as r_0 and not $r_0 - \sigma$. However, in considering the application of equation (2), the effective radius is taken as $r_0 - \sigma$, and the point of hysteresis inception is calculated in the following manner. The desorption pressure p_d is given by

$$p_d = p_0 \exp(-2V\gamma/r_0RT) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

whereas the adsorption pressure p_a is given by

$$p_a = p_0 \exp\{-V\gamma/(r_0 - \sigma)RT\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The condition for $p_d = p_a$ is that $2/r_0 = 1/(r_0 - \sigma)$ or $r_0 = 2\sigma$. This is the radius at the point of hysteresis inception, at which both equations (1) and (2) give the same value for p. It is clear that, unless the effective radii during adsorption and desorption are assumed to be different (*e.g.*, in this case, r_0 and $r_0 - \sigma$), it is impossible to derive any relation between r and σ, thus if the radius is taken as r_0 in both cases, then p_a is *always* $> p_d$. The assumption that $r = r_0$ during desorption but $r = r_0 - \sigma$ during adsorption, though quite inconsistent with the postulate of an initial monolayer, is essential to Cohan's theory in order to predict the value $r_0 = 2\sigma$ which he maintains is in agreement with experiment. Emmett and Cines (*loc. cit.*) have also commented on this inconsistency and have sought to resolve it by assuming that *two* adsorbed layers are present on the walls during adsorption but that only *one* remains during desorption. This makes $r = r_0 - 2\sigma$ for adsorption and $r = r_0 - \sigma$ for desorption, and substitution of these values in (1) and (2) makes $p_a = p_d$ when $2/(r_0 - \sigma) = 1/(r_0 - 2\sigma)$ or $r_0 = 3\sigma$. It is necessary to distinguish carefully between r_0, the true pore radius, and r, the value obtained by the usual method of calculation based on the Kelvin equation. Thus, Cohan's result $r_0 = 2\sigma$ and that of Emmett and Cines ($r_0 = 3\sigma$) correspond to identical *Kelvin* radii, since Cohan puts $r = r_0$ whilst Emmett and Cines put $r = r_0 - \sigma$, hence if $r_0 = 3\sigma$, r must be 2σ.

It is now necessary to see how these arguments are modified by the use of equation (3) instead of (2). Cohan's relation becomes $2/r_0 = 1/(r_0 - \frac{1}{2}\sigma - \sigma)$ or $r_0 = 3\sigma$, whilst the method of Emmett and Cines gives $r = 3\sigma$ or $r_0 = 4\sigma$. If, on the other hand, one assumes that the thickness of the adsorbed layer remains the same during adsorption, then $2/r = 1/(r - \frac{1}{2}\sigma)$ or $r = \sigma$ and $r_0 = 2\sigma$ for one adsorbed layer. This result is clearly not in agreement with experiment since the observed values of r lie between 2σ and 3σ. It therefore seems to be necessary to revert to the less simple view that the number of adsorbed layers does not remain constant and to consider whether this concept has any theoretical basis.

Equilibrium between Adsorbed and Condensed Liquid.—The equilibrium pressure due to capillary condensation in a pore of radius r_0 can only be calculated by means of the Kelvin equation if the number of adsorbed layers (n) is known, since the Kelvin radius $r = r_0 - n\sigma$.

In general, there is no definite and unambiguous method of determining n, although in many systems hysteresis begins when the total amount adsorbed corresponds to roughly twice the amount required to form a complete monolayer. If it be assumed that layer adsorption is followed by capillary condensation as the amount adsorbed increases, then conversely, during desorption the initial stages represent an emptying of pores filled by capillary condensation and a film of liquid several molecules thick will remain behind on the walls during the later stages. The thickness of this layer will depend on the relative magnitudes of the forces causing layer adsorption and those causing condensation. The thicker the adsorbed layer, the larger will be the value of n and hence the smaller the value of r, so that a thick adsorbed layer would at first sight appear to favour a low condensation pressure. This is, of course, true, but the higher the value of n, the greater is the pressure over the multilayer, and presumably a balance between the cohesive and adsorptive forces occurs when the equilibrium pressures due to the two mechanisms are equal. It should therefore be possible to obtain an approximate solution by equating the pressure given by the Kelvin equation to that given by the B.E.T. multilayer adsorption theory for the same value of n. For the purpose of a rough calculation, one of the simple limiting cases of the general B.E.T. equation may be employed. Thus, when the heat of adsorption in the first layer is very much greater than that in the subsequent layers, the amount adsorbed a, expressed as a multiple of the monolayer capacity, is given by

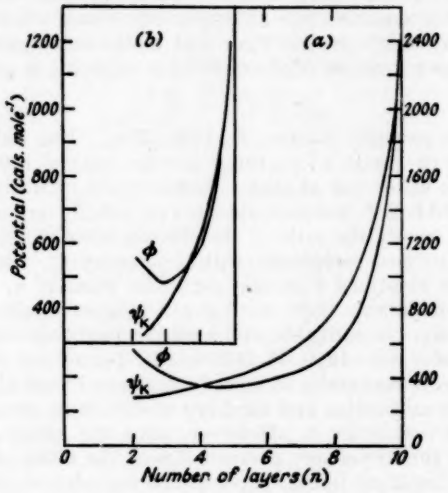
$$a = 1/(1 - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where x is the relative pressure (Foster, *J.*, 1945, 770). The Kelvin equation may be applied by assuming for the product $V\gamma$ a rough average value of 1200, which is quite close to the actual values for water and alcohol. However, the quantity a (which is identical with V/V_m in the original B.E.T. notation) does not necessarily represent the actual number of adsorbed layers but merely the ratio of the amount adsorbed to that which would be required to cover the surface completely with a monolayer. According to the B.E.T. theory, a should not be identified with any particular value of n, but Halsey (*J. Chem. Phys.*, 1948, **16**, 931) maintains that, until a given layer is almost complete, further adsorption in the next layer is negligible, and a similar picture has also been suggested by Tompkins (*Trans. Faraday Soc.*, 1950, **46**, 569) and by Barrer and Robins (*ibid.*, 1951, **47**, 785). It therefore appears reasonable to regard a and n as identical and to argue that the transition between layer adsorption and capillary condensation occurs when equations (1) and (2) give the same value for x. However, once the existence of multimolecular adsorption is admitted, the free-energy decrease during the filling of a pore can no longer be attributed solely to capillary forces, but must be regarded as consisting of *two* parts, one due to the layer adsorption forces and the other due to capillary forces. The original version of the open-pore theory recognised this fact but failed to formulate it quantitatively; Cohan's version, with less justification, since it appeared some years after the B.E.T. theory, ignores it and endeavours to explain hysteresis in terms of equations (4) and (5) alone.

Calculation of Potential Curves for Adsorption and Capillary Condensation.—The logical basis for a quantitative treatment is to find a simple expression for the layer "adsorption potential" (or free-energy decrease) ψ_a, and to combine this with the potential ψ_c due to the cylindrical meniscus effect in order to obtain the *total* free-energy decrease accompanying the formation of a given adsorbed layer. Since ψ_a is initially *high* and falls off as layer formation proceeds, whilst ψ_c is initally *low* and increases as adsorption proceeds (because the radius of the free space remaining in the centre of the pore is decreasing), the *total* potential ϕ $(= \psi_a + \psi_c)$ must pass through a *minimum*. *Before* this minimum is reached, the nth layer is *more* stable than the $(n + 1)$th layer and will be nearly completed before the latter forms appreciably. *Beyond* this minimum, the nth layer becomes *less* stable than the $(n + 1)$th and the pores then fill completely at the pressure corresponding to this potential. Thus, the effect of taking layer adsorption into account is to show that the cylindrical meniscus effect assists layer formation initially and operates as a pore-blocking mechanism only after a number of adsorbed layers have been formed. If true capillary condensation is to be stable, the potential ψ_K given by the Kelvin equation ($\psi_K = RT \log p_0/p = 2V\gamma/r$) cannot be less than the total potential ϕ. ψ_K, like ψ_c, is initially

small, and for the same reasons increases as more layers are formed. When the curve showing the variation of ψ_K with the number of adsorbed layers a, intersects the ϕ–a curve, the pressure over the spherical meniscus of the condensed liquid will be equal to that over the cylindrical meniscus of the adsorbed liquid and no further layer adsorption will occur, since any liquid so held would have a higher pressure, corresponding to the lower potential of the ϕ–a curve (which then lies below the ψ_K–a curve), so that the pore would fill by capillary condensation at this pressure provided that the spherical meniscus were already present. If the pore is open at both ends and has a uniform diameter, or if it is tapering and is not yet blocked at its narrowest part, there will be no meniscus present and further layer adsorption will occur until the minimum of the ϕ–a curve is reached and the pores block completely.

From the typical potential curves plotted in the figure, the derivation of which is described later, it is seen that the point of intersection may lie on either side of the minimum. The basic idea of the new theory is that hysteresis will be observed only when the ψ_K–a and the ϕ–a curve intersect *before* the latter reaches its minimum value. True



capillary condensation becomes *thermodynamically stable* before the necessary meniscus can be formed, so that during adsorption the pores fill at the pressure corresponding to the minimum of the ϕ–a curve, whereas during desorption, when a meniscus has been formed, the same pores do not empty until the pressure corresponding to the point of intersection is reached; this point must necessarily lie at a higher potential than the minimum, and hence correspond to a lower pressure.

During desorption the states represented by that part of the ϕ–a curve lying to the *right* of the minimum are all *unstable* relative to the ψ_K–a curve, and the point of intersection represents the effective minimum potential at which a stable system can exist during pore emptying. The regions where $d\phi/da$ is positive correspond to unstable states (pressure falling with increasing adsorption), which cannot be realised in practice. When the intersection occurs after the minimum is reached, there is in theory a transition point between layer adsorption and capillary condensation but, since this lies in the experimentally unrealisable region, the pores will both empty and fill at the pressure corresponding to the minimum.

Conditions for Occurrence of Hysteresis.—The accurate determination of these potential curves would make it possible to predict whether or not hysteresis would occur in a given system. The simplest, though not necessarily the most exact, basis for quantitative treatment is to use the B.E.T. limiting equation (6) to obtain the variation of ψ_e with the

distance from the surface (which is assumed to be proportional to the number of adsorbed layers). Thus, since $x = 1 - 1/a$, this potential is given by

$$\psi_e = -RT \log x = -RT \log (1 - 1/a) \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The cylindrical meniscus potential is given by (3*a*) as

$$\psi_c = RT \log p_0/p = V\gamma/(r + \sigma/2)$$

where r is the radius of the space remaining *after* the formation of the ath layer. If r is expressed as a multiple $n\sigma$ this becomes

$$\psi_c = 2V\gamma/(2n + 1)\sigma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and the total potential for the formation of the ath layer in a cylinder of total radius $n_0\sigma$ will be

$$\phi = \psi_e + \psi_c = -RT \log (1 - 1/a) + 2V\gamma/(2n + 1)\sigma \quad . \quad . \quad . \quad (9)$$

where $a + n = n_0$. The Kelvin potential, ψ_K, which determines the pressure at which capillary condensation occurs in the *same* capillary when a adsorbed layers are present, is given by equation (1) with the appropriate value of $r = n\sigma$. Hence $\psi_K = 2V\gamma/n\sigma$ and both the potential curves can be calculated for any given pore radius if the constants V, γ, and σ are known. The figure shows two such sets of curves: (*a*) for pore radius 50 Å (10σ) and $V\gamma = 2520$, and (*b*) for pore radius 25 Å (5σ) and $V\gamma = 1260$. In the former, the intersection occurs before the minimum is reached, but in the latter, where the capillary forces are smaller, layer adsorption predominates and the intersection does not occur until after the minimum. The graphical solution of these equations becomes laborious for large values of n_0, but fortunately a simple mathematical solution is possible for the limiting case where both a and n are large, since the logarithmic term in equation (9) can then be expanded and the $(2n + 1)$ factor in the second term replaced by $2n$, giving

$$\phi = (RT/a) + [b/2\sigma(n_0 - a)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where b is the value of $2V\gamma$ expressed in calories per mole. ϕ clearly has a minimum when

$$RT/a^2 = b/2\sigma(n_0 - a)^2$$

or

$$n_0/a = 1 + K^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where $K = b/2RT\sigma$. The point of intersection occurs when $\psi_K = \psi_e + \psi_c$ or

$$b/n\sigma = RT/a + b/2n\sigma$$

whence

$$RT/a = b/2n\sigma \text{ or } n_0/a = 1 + K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Thus in large pores, the ϕ–a curve has a minimum at $a = n_0/(1 + K^{\frac{1}{2}})$ and intersects the ψ_K–a curve at $a = n_0/(1 + K)$. When $K = 1$ the two points coincide and the condition for the intersection to occur before the minimum is reached, and hence for hysteresis to appear, is that the constant K shall be greater than unity.

This surprisingly simple result has been derived by considering a highly idealised but by no means unrealisable system, but even if the majority of systems encountered in practice are more complex, their behaviour must still be partly determined by the same parameter K, which is proportional to $V\gamma/\sigma$.

If V is regarded as $\propto \sigma^3$, then $K \propto \sigma^2\gamma$ and it is evident that the molecular diameter is the chief factor determining the magnitude of K, since γ does not show very wide variations for most organic liquids. The table, which records the results of some rough calculations, shows that K for typical liquids lies between 1·0 and 2·0. It seems that values significantly less than unity will not occur frequently, so that, in large pores, hysteresis should actually be observed with most liquids. This agrees with the work of Broad and Foster, (*J.*, 1946

446) and Brown and Foster (*J.*, 1952, 1139) on ferric oxide gel (pore radius ~30 Å) in which large hysteresis loops were observed with all the liquids examined. However, even in pores of radius 100 Å, the extent of the observed hysteresis areas suggests that only two or three adsorbed layers are present. For such a system, with $r = 20\sigma$ and $K = 1$, equations (11) and (12) predict the formation of ten adsorbed layers, hence the quantitative agree-

Substance	σ (Å)	V	γ	$V\gamma$	K
Water	3·5	18	72	1296	1·4
Methyl alcohol	4·6	40	22	880	0·8
Ethyl alcohol	5·2	58	22	1280	1·0
Ethylenediamine	5·4	67	41	2780	2·0
Benzene	5·9	88	29	2552	1·7
Carbon tetrachloride	6·1	98	26	2550	1·6
Toluene	6·3	107	28	3000	1·8
n-Heptylamine	7·2	151	26	3940	2·1

ment between simple theory and experiment is poor. To remedy this defect it is necessary to have either higher ψ_K or lower ψ_ϵ values, and since the Kelvin equation is unlikely to be seriously in error for large radii, the more probable source of error seems to be in the use of the B.E.T. model for layer adsorption. The limiting B.E.T. equation, which was deliberately chosen for its simplicity, is derived for a plane surface, and its use for adsorption in pores of small radius is not justified. The expansion of the logarithmic term of equation (9) to give RT/a implies that, for large a values, the B.E.T. assumptions are equivalent to a potential which falls off inversely as the distance and corresponds to the existence of long-range adsorption forces.

The simple B.E.T. theory thus overestimates the layer adsorption forces at large distances, and in order to develop a more exact treatment it is necessary to adopt a more realistic model for the adsorption potential. It was suggested by Polanyi (*Trans. Faraday Soc.*, 1932, **28**, 321) that the potential was due to the London dispersion force, which varies inversely as the seventh power of the distance. When integrated over the whole surface, this leads to an inverse-cube law for the potential, and it is noteworthy that this model has recently been adopted by Barrer and Robins (*loc. cit.*) in their attempt to develop an alternative to the B.E.T. theory. It is then necessary to assign, somewhat arbitrarily, a definite value (ψ_0) to the potential in the first layer, which introduces an additional variable into the above equations and it is no longer possible to obtain a simple solution for the limiting case because equation (10) will contain a term in $1/a^3$ and will give a biquadratic equation on differentiation. However, the equations are still easily solved by graphical methods when definite values are assigned to ψ_0, r, and σ, but the operations are laborious. It is hoped to discuss these curves in detail in the next paper of this series. For the present it can be said that when $\psi_0 = 4000$—1000 cals./mole, the ϕ–a curves fall more steeply than those in the figure and intersect the ψ_K curves at smaller values of a corresponding to 2—4 adsorbed layers, thus showing better agreement with experiment.

The graphical solutions so far obtained show that, for both models, in average systems the ψ_K–a curve cuts the ϕ–a curve at or before its minimum when n_0 is large, but that as n_0 decreases (σ being constant) the point of intersection moves forward and has usually passed beyond the minimum by the time n_0 has been reduced to a value of 4—5σ. For two adsorbed layers, this corresponds to a Kelvin radius of 2—3σ and is therefore in agreement with the experimental observations on the point of hysteresis inception.

ROYAL HOLLOWAY COLLEGE (UNIVERSITY OF LONDON),
ENGLEFIELD GREEN, SURREY.

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333. *The Oxidation of Monoethenoid Fatty Acids and Esters. The Union of Gaseous Oxygen with Erucic Acid and Methyl and* n-*Propyl Erucate.*

By J. H. Skellon and P. E. Taylor.

The methods of preparation of highly purified erucic acid and its esters have been studied. Catalytic oxidation of the pure acid and of methyl and *n*-propyl erucate at various temperatures has been investigated, and the nature of the complex changes occurring studied. The oxidations at high temperatures result in rapid hydroperoxide decomposition followed by some dimerisation, and there is evidence that at moderate temperatures the mechanism may follow a different course, as in the case of other monoethenoid fatty acids. The composition of the oxidation products varies considerably with conditions of oxidation and, in oxidations of the esters, the presence of the terminal alkyl group apparently has considerable influence, not only on the rate of entry of the oxygen, but also on that of decomposition of the hydroperoxides.

The disruptive oxidation of erucic acid was first carried out by Dorée and Pepper (*J.*, 1942, 477) who found that oxidation of the *cis*- and the *trans*-form with various oxidising agents cleaved the carbon chain or gave oxido-complexes to a degree varying with the conditions. In the action of gaseous oxygen on erucic acid with and without catalysts at 70° and 120° they concluded that oxido-compounds formed 12—15% of the oxidation products; they suggested that unstable peroxides might be amongst the initial oxidation products, and that from them aldehydic compounds might be formed which polymerised to resistant, brown, oily residues. The formation and decomposition of hydroperoxides of erucic acid and its methyl esters during autoxidations were not investigated by Dorée and Pepper, and the mechanism of autoxidation of this monoethenoid fatty acid has not yet been fully elucidated.

The object of the work now described was to study the catalytic oxidation of pure erucic acid and its methyl and *n*-propyl esters at various temperatures, *viz.*, 55°, 85°, and 120°, and to investigate the nature of the changes taking place at all stages of oxidation—in particular to study hydroperoxide formation and transition at moderate and at high temperature. The oxidations with gaseous oxygen were therefore carried out with catalysts—in the form of soaps of the transition metals—by which means efficient oxidation without dimerisation and polymerisation is obtained comparatively quickly.

For this investigation samples of the acid and its esters were required to be free from polyethenoid fatty acids, the presence of which would modify the course of autoxidation (Hilditch, *Nature*, 1950, **166**, 599).

Separation of erucic acid from the mixed fatty acids of rape seed oil was formerly investigated by Dorée and Pepper (*loc. cit.*). Crystallisation of the mixed acids from alcohol was followed by fractional precipitation of the lead salts from alcoholic solution, insufficient lead acetate for complete precipitation being used (Taufel and Bauschinger, *Z. angew. Chem.*, 1928, **41**, 157).

The separation of erucic acid from rape oil fatty acids involves the removal of (1) saturated fatty acids such as behenic, (2) other monoethenoid fatty acids such as oleic, and (3) more highly unsaturated acids such as linoleic. Saturated fatty acids can be removed by fractional precipitation of the lead salts, but we were not able to secure their complete elimination by a single precipitation (cf. Dorée and Pepper, *loc. cit.*). Oleic and linoleic acids can be eliminated from rape oil acids by repeated crystallisation from alcohol, but the comparatively low melting point of erucic acid (33·8°) limits the useful temperature range. Lead erucate separates as a liquid from hot alcoholic solutions, particularly if lead oleate is also present. Lithium erucate, however, is freely soluble in boiling alcohol, but almost completely precipitated at room temperature. The lithium salts of the saturated acids are also sparingly soluble in alcohol at room temperature, but those of oleic acid and of the more highly unsaturated acids are more soluble.

The method finally adopted was to precipitate the insoluble lithium salts, recrystallise them several times from alcohol, and finally to remove saturated acids by fractional precipitation of the lead salts. The product was pure erucic acid, completely free from polyethenoid acids.

The results of catalytic oxidations of pure erucic acid with uranium erucate as catalyst now show that the general trend of oxidation is similar to that for elaidic acid and its methyl and *n*-propyl esters but with certain modifications. The changes in the observed active-oxygen content during the oxidation of each of these acids and their esters were similar, *i.e.*, a rise to a maximum followed by decomposition, but the percentage of active oxygen corresponding to these maxima was found to be highest in autoxidised propyl erucate, whereas in former work on elaidic acid and its esters (Skellon and Thruston, *J.*, 1949, 1626) highest values were obtained during oxidation of the methyl esters. In the early stages the autoxidations at 120° and 85° were exothermic as the peroxide value was increasing, the thermostatically controlled oven having to be kept a few degrees below the desired temperature with carefully controlled mechanical stirring; this thermal effect was particularly noticeable in the case of erucic acid oxidised at 120° where the peroxides were rapidly decomposed. It is of interest to compare the molar fraction of hydroperoxide present, as measured by the peroxide value, with the fraction oxidised, as measured by the fall in the iodine value (both values being taken at the stage of maximum peroxide-oxygen, content):

At 120°.	Propyl ester	Methyl ester	Acid
(1) Peroxide (molar fraction)	0·325	0·084	0·024
(2) Oxidation (molar fraction)	0·42	0·34	0·24
Ratio (1)/(2)	0·775	0·246	0·100

These results clearly indicate the greater stability of the peroxides of the esters.

The general trend of oxidation of erucic acid and its esters at 85° and 120° appeared to be similar. The changes in peroxide-oxygen content during oxidation of methyl and *n*-propyl erucate at 85° were comparable with those observed during oxidation of methyl and *n*-propyl elaidate at the same temperature (Skellon and Thruston, *loc. cit.*), and the stability of the ester hydroperoxides was again evident. At 55° the rate of oxidation was much slower and the reaction at this temperature probably follows a different course; *e.g.*, oxidation of the acid resulted in an appreciable fall in iodine value with little peroxide formation, whilst in oxidation of the propyl ester the peroxide value changed rapidly with little fall in iodine value.

Molecular-weight determinations indicated some dimerisation at all temperatures. This was confirmed by the fall of the acid value during oxidations of the free acid, indicating that the carboxyl group had taken part in the condensation. The esters increased in viscosity, but the acid, after oxidation at 85° and 120°, gave a product which was liquid at room temperatures. Little carbon dioxide was evolved during the short autoxidations.

The saponification values of the oxidised esters appeared to increase normally with the time of oxidation. There was evidence, however, that a proportion of the oxidation product breaks down to a considerable extent on saponification—probably owing to rupture at the ethenoid linkage.

Influence of the presence of alkyl groups in the molecule was very marked, the peroxide values in ester oxidations always being considerably higher. The results appear to support present views that initial attack at temperatures above 100° takes place directly at the ethenoid linkage, with subsequent migration of the ethenoid linkage and formation and decomposition of isomeric hydroperoxides, resulting in formation of complex oily products containing ketonic groups. It is noteworthy that the ketonic derivatives invariably formed in these and other high-temperature catalytic oxidations of monoethenoid fatty acids and esters are apparently secondary oxidation products of a different character from the unsaturated keto-acids found by Ellis (*Biochem. J.*, 1950, **46**, 129) in autoxidation of oleic and elaidic acid at lower temperatures. The exact nature of the numerous complex products resulting from catalytic oxidation of the various monoethenoid fatty acids and esters is now being systematically investigated, and the results should throw considerable light on later stages of the oxidation mechanism.

Experimental

Preparation of Eurcic Acid.—First preparation. High-grade rape seed oil (800 g.; sap. val., 172·0; I.V., 100·7) was dissolved in alcohol (1 l.) and mixed with a solution of potassium hydroxide (200 g. in 100 ml. of water). After the solution had been heated for 5 hours on a water-bath, the alcohol was distilled off, boiling water added (1 l.), and the liquid acidified; the free fatty acids separated. The aqueous layer was then removed as completely as possible and the fatty acids were washed several times with boiling distilled water. The recovered fatty acids (725 g.; acid val., 187·9; I.V., 108·9) were dissolved in alcohol, heated to boiling, and mixed with a boiling solution of lead acetate (50 g.) in alcohol (200 ml.) containing 1·5% of acetic acid. Next morning, the solid lead salts were filtered off. The mother-liquors were similarly treated and each successive crop of lead salts was converted into free fatty acids, which were washed repeatedly with hot water.

Each batch of free fatty acids was then separated into less soluble and more soluble lead salts by fractional crystallisation. A suitable amount of lead acetate being used, this process was repeated until the following fractions of free fatty acids were obtained:

Fraction	Wt., g.	M. p.	Acid val.	I.V.	Fraction	Wt., g.	M. p.	Acid val.	I.V.
1	25	50°	166	46	5	200	Pasty	—	89·5
2	5	44	166	—			liquid		
3	4	47	166	—	6	79	Clear	—	90
4	105	33	165·9	71			liquid		
					7	70	,,	—	98

After further crystallisation of the lead salts of Fraction No. 4 there were recovered 90 g. of pure erucic acid, m. p. 33·0°, n_D^{40} 1·4512 (Found: acid val, 165·9; I.V., 74·5. Calc. for $C_{22}H_{42}O_2$: acid val., 165·8; I.V., 75·0).

Second preparation (modified process). Fatty acids (730 g.; acid val., 188·9; I.V., 106·9) from rape oil were dissolved in alcohol (2 l.), heated to boiling, and neutralised with a solution of lithium hydroxide. After being kept overnight at room temperature, the insoluble lithium salts were filtered off, recrystallised from aqueous alcohol (1 : 1), and converted into fatty acids by agitation with dilute hydrochloric acid. Recovered crude erucic acid (319 g.) (Found: acid val., 164; I.V., 65·0. Calc. for $C_{22}H_{42}O_2$: acid val., 165·8; I.V., 75·0) was dissolved in hot alcohol (1 l.) and to this was added a solution of lead acetate in alcohol (20 g. in 1 l.) containing a little acetic acid. Next morning, the precipitated lead salts were separated, and the fatty acids (295 g.) recovered from the mother-liquor (Found: acid val., 165·4; I.V., 74·6).

Preparation of Methyl Erucate.—Pure erucic acid (20 g.), methyl alcohol (100 ml.), and concentrated sulphuric acid (2 ml.) were refluxed for 2 hours, excess of alcohol was distilled off, and the residue was poured into water and extracted with light petroleum. After treatment with sodium carbonate solution, the petroleum solution was washed and dried, and the solvent removed; the ester (20 g.) had $n_D^{15\cdot5}$ 1·4575, n_D^{50} 1·449 (Found: acid val., 0·2; sap. val., 159; I.V., 68·6. Calc. for $C_{23}H_{44}O_2$: sap. val., 159·2; I.V., 72·1).

Preparation of Propyl Erucate.—Pure erucic acid (30 g.), *n*-propyl alcohol (100 ml.), and concentrated sulphuric acid (2 ml.) were refluxed for 2 hours. After neutralisation with alcoholic potash, the solution was diluted with water (200 ml.) and extracted with light petroleum. After the extract had been washed and dried, removal of the solvent gave propyl erucate (25 g.), $n_D^{15\cdot5}$ 1·4556, n_D^{50} 1·4429 (Found: acid val., 0·1; sap. val., 147·5; I.V., 63·0. Calc. for $C_{25}H_{48}O_2$: sap. val., 147·5; I.V., 66·7).

Catalytic Oxidations.—Oxidations were carried out in Pyrex boiling tubes, with a glass stirrer of paddle type, a bubbler tube with drawn-off jet for entry of oxygen, and a thermometer. The tubes were inserted through the top of an electric oven (thermostatic control). The oxidations, which were exothermic in the early stages, were sensitive to the rate of stirring, which was therefore kept uniform. The rate of flow of oxygen was also kept constant throughout the series of oxidation (60 bubbles per minute).

(i) *Of erucic acid.* Oxidations of pure erucic acid prepared as detailed were carried out with use of 0·05% of U (as uranium erucate) as catalyst. The results of oxidations at 120°, 85°, and 55° are given in Table 1. All peroxide values are expressed as active oxygen (%). There was slight reduction of Fehling's solution at the end of the heating at 120° and 85°, but none after that at 55°; the molecular weights (by Rast's method) of the final products were 378, 354, and 400, respectively (Calc. for $C_{22}H_{42}O_2$: *M*, 338).

TABLE 1. *Catalytic oxidation of erucic acid.*

At 120°.	Time (hours)	1	2	3	4	5	6	7
	I.V.	69·3	61·3	57·3	—	46·9	39·7	36·5
	Acid val.	165	157	152	151	145	—	143
	Active oxygen, %	0·03	0·08	0·11	0·09$_4$	0·06	0·026	0·017
	n_D^{50}	1·4525	1·4530	1·4540	1·4562	1·4569	1·4577	1·4582
At 85°.	Time (hours)	1	2	4	8	12	16	21
	I.V.	67·2	64·4	63·0	55·7	50·1	45·8	42·3
	Acid val.	159	157·5	158	153	150	149	144
	Active oxygen, %	—	0·17	0·175	0·30	0·29	0·36	0·17
	n_D^{50}	1·4507	1·4512	1·4517	1·4531	1·4539	1·4536	1·4545
At 55°.	Time (hours)	4	8	12	16	20	23·5	
	I.V.	65·1	64·2	62·4	51·2	42·1	—	
	Acid val.	160	160	159	157	162	161	
	Active oxygen, %	0·05	0·06	0·09	0·105	0·112	—	
	n_D^{50}	1·4514	1·4522	1·4514	1·4516	1·4516	—	

(ii) *Of methyl erucate.* This was carried out under the same conditions as for the acid, and the results are given in Table 2. Reduction of Fehling's solution was rapid after the final heating at 120°, slight after that at 85°, and nil after that at 55°, and the molecular weights (Rast's method) were 352, 362, and 346, respectively (Calc. for $C_{23}H_{44}O_2$: *M*, 352).

TABLE 2. *Catalytic oxidation of methyl erucate.*

At 120°.	Time (hours)	1	2	3	4	5	7	7·75
	I.V.	63·8	61·3	56·6	53·4	47·7	39·1	29·3
	Sap. val.	165	175	177	—	196	202	212
	Active oxygen, %	0·10	0·18	—	0·32	0·35	0·24	0·17
	n_D^{50}	—	1·4588	1·4594	1·4599	1·4598	1·4610	1·4613
At 85°.	Time (hours)	1	2	4	8	12	16	21
	I.V.	64·2	64·7	64·3	60·9	59·4	57·6	51·3
	Sap. val.	161	161	162	163	162·5	164	173
	Active oxygen, %	—	0·10	0·10	0·16	0·19	0·38	0·60
	$n_D^{15·5}$	1·4579	1·4580	1·4581	1·4581	1·4583	1·4587	1·4588
At 55°.	Time (hours)	4	8	12	16	20	23·5	
	I.V.	63·8	64·8	63·7	63·7	62·3	63·4	
	Sap. val.	166	172	161	164	172	165	
	Active oxygen, %	0·035	0·038	0·043	0·060	0·052	—	
	$n_D^{15·5}$	1·4577	1·4568	1·4573	1·4569	1·4575	1·4572	

(iii) *Of propyl erucate.* The results obtained under the same conditions are given in Table 3. The reduction of Fehling's solution by the final products of the runs at 120°, 85°, and 55° was rapid, slight, and negative, respectively, and the corresponding values of *M* (by Rast's method) were 362, 368, and 420 (Calc. for $C_{25}H_{48}O_2$: *M*, 380).

TABLE 3. *Catalytic oxidation of propyl erucate.*

At 120°.									
Time(hours) ...	2	4	6	8	10	12	17	21	23
I.V.	57·6	55·5	50·6	49·1	44·0	38·4	—	33·2	—
Sap. val.	140	142	156	166	183	192·5	244	275	—
Active oxygen, %	0·44	0·65	0·90	1·26	1·2	1·05	1·08	0·76	0·49
$n_D^{15·5}$	1·4565	1·4574	1·4579	1·4581	1·4584	1·4590	1·4603	1·4611	—
At 85°.									
Time (hours) ...	1	3	6	9	12	15	18	20	23
I.V.	62·0	62·0	58·7	59·8	57·2	56·4	51·4	—	45·0
Sap. val.	149	156	161	167	169	163	145	—	161
Active oxygen, %	0·03	0·07	0·16	0·25	0·34	0·50	0·51	0·66	0·69
$n_D^{15·5}$	1·4567	1·4562	1·4569	1·4573	1·4577	1·4579	1·4580	—	1·4580
At 55°.									
Time (hours) ...	1	2	4	8	12	16	20	24	
I.V.	—	—	60·9	60·5	61·5	—	62·7	62·2	
Sap. val.	—	—	146	147	150	150	156	—	
Active oxygen, %	0·05	0·07	0·17	0·26	0·20	0·35	0·20	0·11	
$n_D^{15·5}$	—	—	1·4569	1·4570	1·4569	1·4516	—	1·4567	

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334. *The Catalysed Reactions of Simple Aromatic Compounds with Ethylenic Systems. Part II.* Cinnamic Acid.*

By J. F. J. Dippy and J. T. Young.

The experimental conditions for the addition of benzene, toluene, anisole, fluorobenzene, chlorobenzene, and bromobenzene to cinnamic acid under the influence of anhydrous aluminium chloride have been investigated. The aromatic residue provided by the solvent is added at the β-carbon of the unsaturated acid in all cases, leading mostly to substantial yields of ββ-diphenylpropionic acids with the substituent in the *p*-position (uncertainty existing in the case of toluene). With chlorobenzene alone reaction proceeds further to give ββ-di-*p*-chlorophenylpropionic acid whereby the original phenyl group has been replaced by chlorophenyl. The same product was also obtained by the action of chlorobenzene on the unsubstituted diphenylpropionic acid, and, in this case, the fate of the displaced phenyl groups was established by the isolation of benzene.

Addition of simple aromatic compounds to unsaturated carboxylic acids in the presence of acid catalysts has been the subject of inquiry by several workers, most attention having been directed to long-chain aliphatic compounds. In a review of cases where anhydrous aluminium chloride was the catalyst, Thomas (" Anhydrous Aluminium Chloride in Organic Chemistry," 1941, pp. 468—469) observes that, except in the reactions with oleic acid, the reports are scanty and often contradictory; in some cases identification of the products is not completely satisfactory and, furthermore, the yields and the experimental conditions are often not recorded.

In the present paper, therefore, some catalysed reactions of cinnamic acid with simple aromatic compounds are reported. Cinnamic acid was first used in reactions of this kind by Liebermann and Hartmann (*Ber.*, 1891, **24**, 2582; 1892, **25**, 957, 2124); both the *trans*- and the *cis*-acid were treated with phenols, benzene, and *m*-xylene in the presence of concentrated sulphuric acid, leading to addition of the aryl group to the β-carbon of the acid. Karsten (*Ber.*, 1893, **26**, 1579) obtained similar results with toluene; Eijkman (*Chem. Weekblad*, 1907, **4**, 727; 1908, **5**, 655) in a systematic examination of the reactions of various unsaturated acids and lactones, with benzene (and, in a few cases, with toluene), using anhydrous aluminium chloride as catalyst, also reported that cinnamic acid and benzene gave ββ-diphenylpropionic acid, and Wislicenus and Eble (*Ber.*, 1917, **50**, 250) obtained this acid by similar means in almost quantitative yield at room temperature. Nevertheless, Marcusson (*Z. angew. Chem.*, 1920, **33**, 234) denied the occurrence of such reactions in systems where the double bond is adjacent to the carboxyl group, suggesting that, in these acids, the catalyst does not add to the double bond, thereby precluding condensation with benzene. Eijkman's general findings for cinnamic acid, however, have been confirmed by Pfeiffer and Waal (*Annalen*, 1935, **520**, 185), Koelsch *et al.* (*J. Amer. Chem. Soc.*, 1943, **65**, 59), Allen and Gates (*ibid.*, p. 422), and Dey and Ramanathan (*Proc. Nat. Inst. Sci. India*, 1943, **9**, 193), all using anhydrous aluminium chloride as the catalyst, and by Simons and Archer (*J. Amer. Chem. Soc.*, 1939, **61**, 1521) with anhydrous hydrogen fluoride. Widely varying reaction conditions and yields were recorded by these workers, so we sought to determine the most favourable method as well as to confirm that addition of the aryl group occurs exclusively at the β-position. The effect of using monosubstituted derivatives of benzene in place of benzene was also investigated, and our results are summarised in the Table.

The results for Expt. 1 agree in every respect with those of Wislicenus and Eble and of Eijkman (*locc. cit.*). The only product isolated by fractional crystallisation was ββ-diphenylpropionic acid. Since this acid is of synthetic value, we compared the effectiveness of Wislicenus and Eble's procedure with that of Pfeiffer and Waal (*loc. cit.*, and quoted in Shirley's " Preparation of Organic Intermediates," 1951, p. 137) (Expt. 2 in the Table).

* Part I, *J.*, 1951, 1415.

The yields by the two processes were similar, but only 1½ hours is required for completion of reaction in Expt. 1 as against 12 hours in Expt. 2.

Expt. no.	Benzenoid addendum	Procedure (see p. 1819)	Product	Yield (pure), %
1	C_6H_6	(*a*)	$CHPh_2{\cdot}CH_2{\cdot}CO_2H$	87
2	C_6H_6	*	$CHPh_2{\cdot}CH_2{\cdot}CO_2H$	91
3	PhCl	(*c*)	p-$C_6H_4Cl{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	51
4	PhCl	(*d*)	$(p$-$C_6H_4Cl)_2CH{\cdot}CH_2{\cdot}CO_2H$	22
5	PhBr	(*d*)	p-$C_6H_4Br{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	5
6	PhF	(*d*)	p-$C_6H_4F{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	30
7	PhOMe	(*b*)	p-$C_6H_4(OMe){\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	37
8	PhMe	(*a*)	$C_6H_4Me{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	44
9	PhMe	(*b*)	$C_6H_4Me{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$	37

* By the procedure of Pfeiffer and Waal (*loc. cit.*).

The experimental details given by Marcusson (*loc. cit.*) for αβ-unsaturated acids are vague and his failure to obtain normal addition products could have been due to the use either of too high a reaction temperature, or of too little or too much catalyst. It is known that high temperatures promote cyclisation of these products of addition: *e.g.*, Koelsch *et al.* (*loc. cit.*) obtained 39% of 3-phenylindanone by heating cinnamic acid with benzene and 3·3 mols. of aluminium chloride for five hours. Eijkman first used an elevated temperature (*loc. cit.*, 1907) whereby he obtained indifferent results, but later (*loc. cit.*, 1908) claimed better success with milder conditions. Again, Schmidt (*J. Amer. Chem. Soc.*, 1930, **52**, 1172) found that the production of phenylstearic acid, by heating oleic acid and benzene in the presence of aluminium chloride, proceeded most favourably when equimolecular amounts of oleic acid and catalyst were used; excessive amounts of catalyst, or prolonged heating, gave products having low neutralization equivalents, but, on the other hand, with less than 0·33 mol. of catalyst little reaction occurred. Our own experience is similar because, in the presence of about 0·6 mol. of the catalyst, benzene does not add to cinnamic acid even after several days. There are indications that the aluminium chloride first added reacts with the carboxyl group leading to hydrogen chloride, and involving two molecular proportions of cinnamic acid and one of aluminium chloride.

The best conditions for promotion of the addition of a simple aromatic compound to cinnamic acid in the presence of aluminium chloride to give a ββ-diarylpropionic acid thus appear to be (i) the use of rather more than one mol. of the catalyst relative to the unsaturated acid (in practice, 1·5—2 mols. of technical anhydrous aluminium chloride is used, the reaction being cooled until addition of the catalyst is complete), and (ii) a relatively low reaction temperature (normally, the reaction mixtures are kept at room temperature, except where halogenated benzenes are used).

Anhydrous boron trifluoride was found to be ineffective as catalyst, recalling that Colonge and Pichat (*Bull. Soc. chim.*, 1949, Jan., p. 177; May, p. 142) showed boron trifluoride to be of no use in catalysing additions of benzenoid compounds to unsaturated ketones.

When cinnamic acid was treated with an excess of a *mono-substituted benzene* in the presence of anhydrous aluminium chloride (procedures *a*, *b*, and *c*) addition again occurred (Expt. 3 and 5—9), a *p*-substituted ββ-diphenylpropionic acid being produced. With cinnamic acid and chlorobenzene, however, we have succeeded in isolating also a *pp'*-disubstituted ββ-diphenylpropionic acid, in which an aryl group derived from the solvent has replaced the β-phenyl group of the initial addition product. For the addition reaction the conditions used by Wislicenus and Eble (*loc. cit.*) with benzene were ineffective, but when the reaction mixture was kept at 30—45° for one hour after introduction of the catalyst [procedure (*c*)], normal addition took place giving β-*p*-chlorophenyl-β-phenylpropionic acid. The product of subsequent replacement, *i.e.*, ββ-di-*p*-chlorophenylpropionic acid, was then obtained by prolonging the reaction for 2—3 days [procedure (*d*), Expt. 4]. It is noteworthy in this connection that Fuson, Kozacik, and Eaton (*J. Amer. Chem. Soc.*, 1933, **55**, 3799) with chlorocinnamic acids and chlorobenzene also used an elevated temperature in obtaining the product of replacement, whereas Allen and Gates

(*loc. cit.*) secured only partial addition of bromobenzene to cinnamic acid at room temperature.

We also obtained ββ-di-*p*-chlorophenylpropionic acid from chlorobenzene and ββ-diphenylpropionic acid at room temperature in the presence of a large excess of aluminium chloride (*ca.* 10 mols.) with added hydrogen chloride. This is consistent with the results of Fuson and his co-workers with αβ-unsaturated ketones (*J. Amer. Chem. Soc.*, 1934, **56**, 687, 1241, 2103) where the step-wise nature of the addition and replacement reactions of Friedel–Crafts type was first demonstrated. Furthermore, we have established the fate of the displaced phenyl groups in the foregoing reaction by isolating benzene from the residual solvent after removal of the resultant acid. The only evidence concerning this aspect of the general problem hitherto provided was that of Fuson, Kozacik, and Eaton (*loc. cit.*) who identified bromobenzene in the solvent layer from the reaction between *p*-bromobenzylidenequinaldine and benzene by its conversion into a Grignard compound followed by treatment with phenyl *iso*cyanate to give benzanilide as the final product.

With fluorobenzene and bromobenzene we isolated β-*p*-fluoro- and β-*p*-bromo-phenyl-β-phenylpropionic acids but not the products of subsequent replacement. Anisole is added at the same temperature as benzene; no replacement of the phenyl group took place even after 3 days.

It was expected that toluene would react at least as readily as benzene. Addition alone has been shown to ensue, β-phenyl-β-tolylpropionic acid being obtained in good yield (Expt. 8) but apparently consisting of an intractable mixture of isomerides. Under conditions designed to promote the formation of the ultimate replacement product (Expt. 9) cinnamic acid and toluene yielded the same acid mixture although in diminished yield and accompanied by tars. Under similar conditions *p*-xylene gave evidence of some addition but phenylxylylpropionic acid could not be isolated.

Addition of the aryl group to the β-carbon atom in these reactions is consistent with the well-known additions to acrylic acid which do not conform to the Markownikoff rule on account of the strong polar influence of carboxyl group adjacent to the double bond. In cinnamic acid the opposing ambipolar phenyl group is a secondary influence on orientation of the addendum. This reaction has been described by Fuson, Kozacik, and Eaton (*loc. cit.*) as "a reversible Friedel–Crafts addition," and they suggest that the explanation of the replacement product should also involve equilibria of this kind. It is significant, however, that all recorded cases of this replacement involve the *gem*-diaryl group, and more investigation is needed on this and other aspects of the problem before any certain light can be shed on the course followed by either of the processes.

Experimental

Reactions of Benzenoid Compounds with Cinnamic Acid. Methods of Procedure.—Pure, dry reagents were employed throughout and the anhydrous aluminium chloride, of commercial quality (supplied by British Drug Houses Ltd., and Imperial Chemical Industries Limited), was stored in sealed bottles; different samples were given batch numbers, and, as far as possible, related experiments were conducted with catalyst of one batch. The reactions were carried out in all-glass apparatus under anhydrous conditions. The following procedures were employed:

(*a*) (Cf. Wislicenus and Eble, *loc. cit.*) The acid was stirred with excess of the benzenoid solvent, cooled to 0—5°, and powdered anhydrous aluminium chloride (about 1·8 mols. with respect to the acid) added in portions to the mixture, the temperature not rising above 10°. After 1 hour's stirring the whole was poured on crushed ice and hydrochloric acid to halt the reaction.

(*b*) As in (*a*), but after addition of the catalyst, the mixture was kept at room temperature for 2—3 days with stirring at intervals.

(*c*) As in (*a*), but after addition of the catalyst, the mixture was warmed to 30—45° for 1 hour, then poured directly on ice and hydrochloric acid.

(*d*) As in (*c*), but, after the heating, the mixture was set aside at room temperature for 2—3 days with occasional stirring.

Isolation of the Acid Product.—The reaction mixture produced by any of the above procedures was usually almost black and contained undissolved aluminium chloride. After the

reaction had been halted, the mixture was stirred for at least 10 minutes to hydrolyse any catalyst complexes. The pale yellow solvent layer then usually separated sharply, and after its removal the aqueous acid layer was extracted twice with further solvent. The pooled extracts were washed twice with water, and the solvent was removed in steam (this is preferable to alkaline extraction of the solvent which tends to produce emulsions). The residue from the steam-distillation (usually brown) was dissolved in hot aqueous sodium carbonate, and the solution was filtered (if much solid remained) and clarified with charcoal. The deposit from the acidified filtrate was filtered off or extracted with ether. A high yield of almost colourless crude acid (*ca.* 90%) was obtained as a rule, but purification of this was mostly difficult. Several crystallisations were usually necessary (the acids tending to separate as oils); in obstinate cases, the acid was purified by distillation of the methyl ester.

Confirmation of Identity.—Equivalents were determined by direct titration (on the semi-micro-scale) with barium hydroxide solution. The presence of halogen was shown by application of the calcium oxide incineration test. Oxidation to the corresponding benzophenone was usually effected by boiling 1 g. of the acid for 6 hours with aqueous potassium permanganate (4 g. in 80 ml. of water), whereupon the ketone was recovered by steam-distillation.

Cinnamic Acid and Benzene.—Procedure (*a*). Cinnamic acid (15 g.), benzene (220 ml.), and aluminium chloride (25 g.) were used. As the catalyst was added the mixture became bright yellow and later dark brown, the acid dissolved, and hydrogen chloride was evolved. After working up, the eventual aqueous sodium carbonate extract was acidified, and the precipitate, on recrystallisation from ethanol, gave ββ-diphenylpropionic acid (20 g., 87%) in fine needles, m. p. 155° (Pfeiffer and Waal, *loc. cit.*, give m. p. 154—155°) (Found: equiv., 225. Calc. for $C_{15}H_{14}O_2$: equiv., 226). No other product could be isolated. The identity of the acid was confirmed by preparation of the amide, m. p. 125°, and by admixed m. p. with an authentic sample synthesised by an unambiguous route *via* a Reformatsky condensation.

By the method of Pfeiffer and Waal (loc. cit.). Cinnamic acid (15 g.) and benzene (180 ml.) were stirred together and cooled to <10°. Anhydrous aluminium chloride (6 g.) was added, and the mixture kept at 10—15° for 10 hours (with stirring), a further 24 g. of aluminium chloride being added, in four equal portions during this time (making a total of 30 g. of the catalyst, *i.e.*, about 2·2 mols. with respect to the acid). The whole was then poured into 300 ml. of water and 60 ml. of hydrochloric acid, and the mixture well shaken. The benzene was removed in steam, and the pale-brown, granular residue, after being heated with 600 ml. of water, was dissolved in aqueous sodium carbonate, and the solution was filtered. Acidification gave a precipitate which, after treatment again with water (600 ml.), gave ββ-diphenylpropionic acid (21 g., *i.e.*, 91%).

Procedure (*b*), *except that* 6 *days' storage was allowed.* Cinnamic acid (5 g.), benzene (70 ml.), and aluminium chloride (2·8 g., *ca.* 0·6 mol. with respect to the acid) yielded cinnamic acid (3·5 g.) as the only product.

Cinnamic Acid and Chlorobenzene.—Procedure (*c*). Cinnamic acid (10 g.), chlorobenzene (130 ml.), and aluminium chloride (16·5 g.) were used. As the temperature was raised, after addition of the catalyst, vigorous evolution of hydrogen chloride occurred at about 11°. The product was worked up by the standard method and separated as an oil which was then extracted with benzene. The residue from the dried extract crystallised from light petroleum (b. p. 100—120°) (11·6 g.; m. p. 82—83°), and a further 4·15 g. were recovered from the mother-liquor. Recrystallisations from both light petroleum (b. p. 100—120°) and aqueous ethanol gave β-*p*-chlorophenyl-β-phenylpropionic acid, m. p. 95° (Bergmann *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 1612, record m. p. 108°) (Found: C, 69·1; H, 5·2; Cl, 13·5%; equiv., 258. Calc. for $C_{15}H_{13}O_2Cl$: C, 69·1; H, 5·1; Cl, 13·6%; equiv., 261). The orientation was confirmed by oxidation (of 2 g.) with aqueous potassium permanganate to 4-chlorobenzophenone (0·30 g.), m. p. 73—74° (Schaum and Unger, *Z. anorg. Chem.*, 1924, **132**, 90, give m. p. 75·5—76°).

Procedure (*a*). Cinnamic acid alone was recovered.

Procedure (*d*). This was applied to the same quantities. The crude product (18·9 g.), isolated as usual, was thrice recrystallised from ethanol, to give ββ-di-(*p*-chlorophenyl)propionic acid as prisms (3·0 g.), m. p. 189—190° (Fuson *et al.*, *J. Amer. Chem. Soc.*, 1933, **55**, 3799, give m. p. 188—189°) (Found: equiv., 291. Calc. for $C_{15}H_{12}O_2Cl_2$: equiv., 295). From the mother-liquor, more of the acid (1·3 g.) was recovered. Oxidation of the acid (1 g.) with aqueous potassium permanganate gave 4 : 4′-dichlorobenzophenone (0·5 g.), m. p. 145° (Cook and Chambers, *J. Amer. Chem. Soc.*, 1921, **43**, 334, give m. p. 146°).

Cinnamic Acid and Bromobenzene.—Procedure (*d*). Cinnamic acid (5 g.) was treated with bromobenzene (80 ml.) and aluminium chloride (8·25 g.). On warming, after addition of the

catalyst at 4°, no evolution of hydrogen chloride was perceptible until about 12°. The crude product was isolated by the standard method, using ether-extraction in the final stage, and consisted of a yellow oil containing some solid (8·7 g.). Treatment with ethanol gave crystals (3·3 g.) which on recrystallisation twice from light petroleum (b. p. 100—120°)–benzene gave small colourless prisms (1·5 g.), m. p. 116—118°. Four further recrystallisations from aqueous ethanol containing a little acetic acid gave β-*p*-bromophenyl-β-phenylpropionic acid (0·5 g.), m. p. 130—130·5° (Found: C, 58·3; H, 4·2; Br, 26·5%; equiv., 303. Calc. for $C_{15}H_{13}O_2Br$: C, 59·0; H, 4·3; Br, 26·2%; equiv., 305) (cf. Allen and Gates, *loc. cit.*, m. p. 107—108°). From the mother-liquors impure acid (1·65 g.) was obtained. Oxidation of this material with aqueous potassium permanganate gave *p*-bromobenzophenone, m. p. 76—77° (cf. Schöpff, *Ber.*, 1891, **24**, 3766, m. p. 79—80°).

Cinnamic Acid and Fluorobenzene.—Procedure (*d*). From cinnamic acid (2 g.), fluorobenzene (25 ml.), and aluminium chloride (3·3 g.), appreciable evolution of hydrogen chloride occurred during the addition of the catalyst. The acid product was isolated as usual and extracted with ether, giving a pale-yellow, viscous oil (3·25 g.). Recrystallisations from benzene–light petroleum (b. p. 60—80°) gave β-*p*-fluorophenyl-β-phenylpropionic acid (1 g.) as prisms, m. p. 111° (Bergmann *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 1612, give m. p. 118°) (Found: C, 73·7; H, 5·0%; equiv., 244. Calc. for $C_{15}H_{13}O_2F$: C, 73·7; H, 5·4%; equiv., 244). Oxidation with aqueous potassium permanganate gave an extremely volatile, colourless ketone (m. p. 46°) in small yield, probably *p*-fluorobenzophenone (Koopal, *Rec. Trav. chim.*, 1915, **34**, 115, records m. p. 52°).

Cinnamic Acid and Anisole.—Procedure (*b*). From cinnamic acid (2·5 g.), purified anisole (35 ml.), and aluminium chloride (4·2 g.), the product (4·7 g.) was isolated by the normal method and after recrystallisations from benzene–light petroleum (b. p. 100—120°) gave β-*p*-methoxyphenyl-β-phenylpropionic acid in prisms (1·6 g.), m. p. 122° (Bergmann *et al.*, *loc. cit.*, give m. p. 122°); the m. p. was raised to 128—129° by drying over phosphoric oxide at 110° (Found: C, 74·9; H, 5·2%; equiv., 262, 264. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·3%; equiv., 256). Further acid (1·1 g.) was recovered from the mother-liquors. No product was isolated when this acid was oxidised by aqueous potassium permanganate.

Cinnamic Acid and Toluene.—Procedure (*a*). Cinnamic acid (5 g.), toluene (70 ml.), and aluminium chloride (8·3 g.) became dark brown, and hydrogen chloride was evolved at about 8°. The crude acid product (8·9 g.), isolated by the usual method, with ether-extraction in the last stage, was recrystallised twice from ethanol and once from light petroleum (b. p. 100—120°) and had m. p. 129° (1·5 g.), a further 2·6 g. (m. p. 118°) being recovered from the mother-liquors. β-Phenyl-β-*o*-, -*m*-, and -*p*-tolylpropionic acid melt at 129°, 109°, and 140° respectively according to von Braun, Manz, and Reinsch (*Annalen*, 1929, **468**, 277). In an attempt further to purify the phenyltolylpropionic acid the *methyl* ester (1·8 g.; b. p. 185—187°/5 mm.; from 2·6 g. of acid) was prepared (Found: C, 80·5; H, 7·3. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The acid (0·83 g.) obtained by hydrolysis of the ester (0·84 g.) on recrystallisation successively from ethanol, aqueous acetic acid, and light petroleum (b. p. 100—120°) had m. p. 123° (Found: equiv., 244. Calc. for $C_{16}H_{16}O_2$: equiv., 240). The orientation is uncertain since oxidation under three different conditions failed to yield an identifiable product.

It is likely that some migration of the methyl group had occurred under the influence of the catalyst, leading to an intractable mixture of isomers. The preparation of the addition product was repeated, and after several recrystallisations a specimen of the same acid, m. p. 120° (equiv., 246), was obtained.

Procedure (*b*).—Half the quantities of the foregoing reactants, when poured on ice–hydrochloric acid, yielded a tarry product. The whole was worked up by the normal method and the crude acid obtained as a colourless solid (2·7 g.), m. p. 110°; after recrystallising once from alcohol, this yielded colourless crystals (1·5 g.), m. p. 120°. Further purification through the methyl ester (0·92 g.), b. p. *ca.* 180°/3 mm., led to a specimen (0·35 g.), m. p. 122—123° (mixed m. p. with a specimen from the preceding experiment, 122—123°).

Cinnamic Acid and Benzene in the Presence of Anhydrous Boron Trifluoride.—Cinnamic acid (5 g.) was added to benzene (150 ml.) saturated with dry boron trifluoride (*ca.* 6 g. of BF_3, 2·7 mols. with respect to the acid). The whole was well shaken; the solution became yellow but there was no temperature rise. Next morning the mixture was poured into ice–water, and the solvent layer then washed with water and extracted twice with sodium carbonate solution. The extract on acidification yielded cinnamic acid (3·8 g.).

Reaction of ββ-*Diphenylpropionic Acid with Chlorobenzene.*—ββ-Diphenylpropionic acid (2 g.) was dissolved in chlorobenzene (300 ml.) and stirred with powdered anhydrous aluminium

chloride (12 g., *ca.* 10 mols.), and dry hydrogen chloride gas passed in to saturation (20 minutes). After 20 hours with occasional stirring, the mixture (almost black) was thoroughly mixed with ice and hydrochloric acid. The crude product (2 g.), isolated in the usual manner, was thrice recrystallised from ethanol, to give ββ-di-*p*-chlorophenylpropionic acid (0·35 g.), m. p. and mixed m. p. 190° (Found: equiv., 293. Calc. for $C_{15}H_{12}O_2Cl_2$: equiv., 295). Further acid (0·13 g.) was recovered from the mother-liquor.

The above experiment was repeated with 10 g. of ββ-diphenylpropionic acid. After removal of the eventual acid product with aqueous sodium carbonate, the solvent layer was washed twice with water, dried ($CaCl_2$), and distilled. The first fraction (1·9 ml.), b. p. 79·2—79·5°/760 mm., was identified as benzene by conversion into *m*-dinitrobenzene. The distillation apparatus incorporated a heated 2-ft. column of Fenske helices with a total-condensation, variable take-off head of Whitmore and Lux pattern. Its efficiency for the object in hand was initially demonstrated by the successful fractionation of a prepared mixture of purified benzene (16 ml.) and chlorobenzene (484 ml.). From this, benzene (9·1 ml.) was recovered as a first fraction, b. p. 79·7—80·0°/760 mm. (all b. p.s recorded here have been corrected to 760 mm. pressure).

The chlorobenzene used for these experiments was purified by refluxing it with anhydrous aluminium chloride, washing, drying, and fractionation.

CHELSEA POLYTECHNIC, LONDON, S.W.3. [*Received, January 15th*, 1952.]

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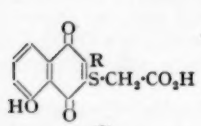
335. *The Reduction of Juglone.*

By R. H. THOMSON.

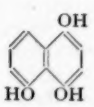
The yellow compound previously obtained by hydrogenolysis of 3-carboxymethylthiojuglone (I; R = H) with Raney nickel is shown to be 5 : 8-dihydroxy-1-tetralone (VI; R = H) arising by further reduction of α-hydrojuglone (II). Similar treatment of β-hydrojuglone gives the keto-alcohol (IV).

IN the preparation of plumbagin (2-methyljuglone) by hydrogenolysis of (I; R = Me) with Raney nickel, a small amount of a yellow by-product (*A*), m. p. 164°, was isolated (*J.*, 1951, 1237). A similar yellow compound (*B*), m. p. 184°, was also obtained by hydrogenolysis of 3-carboxymethylthiojuglone (I; R = H). The unusual formation of coloured compounds by reduction of naphthaquinones seemed worthy of further investigation, and the structure of the more accessible substance (*B*) has now been established.

In the hydrogenolysis of (I; R = H) the quinone is very rapidly reduced to the quinol, and as (*B*) contains no sulphur it must be derived from α-hydrojuglone (II). This was confirmed when (*B*) was obtained by refluxing (II) (or juglone) with a large excess of Raney nickel in alcohol, ethyl acetate, or light petroleum. Yields were usually extremely small and consistent results could not be obtained. It was then found that (*B*) could be prepared by catalytic hydrogenation of juglone with Raney nickel at ordinary temperatures and pressures, and this method, although tedious, was reliable. After rapid uptake of 1 mol. of hydrogen, hydrogenation continued slowly, about 0·5 mol. being absorbed in 2—3 days. The reaction was even slower with Adams's catalyst and did not proceed at all in glacial acetic acid.



(I)



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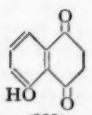

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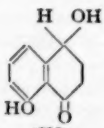
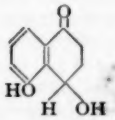


(IV)



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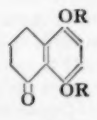
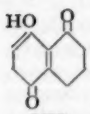


(VI)

The compound (*B*) forms a bright yellow solution in dilute sodium hydroxide solution, the colour being weaker in dilute sodium carbonate solution, and gives a transient blue-green colour with ferric chloride. It forms a diacetate, a methyl ether, a phenylurethane, and a *p*-nitrophenylhydrazone. Elementary analyses of (*B*) and its derivatives were very misleading initially and it was necessary to sublime most of the compounds in a high

vacuum before satisfactory results could be obtained. The empirical formula is $C_{10}H_{10}O_3$, *i.e.* $C_{10}H_8O_3$ (II) + 2H. When juglone is refluxed with Raney nickel in alcohol the odour of acetaldehyde can be detected. It is known that Raney nickel will catalyse such oxidations in the presence of a hydrogen acceptor, usually a ketone, which is thereby reduced to a secondary alcohol, or further (Kleiderer and Kornfeld, *J. Org. Chem.*, 1948, **13**, 455). A suitable ketone could arise by isomerisation of α-hydrojuglone (II) to the β-form (III) (see *J.*, 1950, 1737). However catalytic reduction of β-hydrojuglone over Raney nickel afforded a new $C_{10}H_{10}O_3$ compound. This substance gave a red-violet ferric colour, formed a *p*-nitrophenylhydrazone, did not react with diazomethane, and on dehydration yielded 1 : 8-dihydroxynaphthalene. The keto-alcohol is therefore (IV). Small amounts of this compound were occasionally isolated after juglone had been refluxed with Raney nickel in ethyl acetate or light petroleum, and could be obtained by a similar treatment of β-hydrojuglone. Since (IV) is colourless, the isomer (V) must also be colourless. Thus (*B*) is neither (IV) nor (V) and must therefore arise by hydrogenation of the monohydroxylated ring of (II). Of the structural possibilities only (VI; R = H) could account for the properties of (*B*). Cyclisation of γ-(2 : 5-dimethoxyphenyl)butyric acid yielded 5 : 8-dimethoxy-1-tetralone (VI; R = Me) which, on demethylation, gave 5 : 8-dihydroxy-1-tetralone (VI; R = H), identical with (*B*). The compound (*A*) is consequently 5 : 8-dihydroxy-6-methyl-1-tetralone. The reduction of a naphthol to a tetralone is not new. 1-Tetralone can be obtained by hydrogenation of 1-naphthol at elevated temperatures and pressures with a nickel catalyst, and under similar conditions 1 : 5- and 1 : 8-dihydroxynaphthalene have been converted into the corresponding hydroxytetralones (Schroeter, G.P. 352,720; *Annalen*, 1922, **426**, 83). Hydroxytetralones have also been obtained by reduction of 1 : 5- and 1 : 6-dihydroxynaphthalene with Raney nickel alloy and sodium hydroxide solution (Papa, Schwenk, and Breiger, *J. Org. Chem.*, 1949, **14**, 366).

A curious feature of 5 : 8-dihydroxytetralone is its failure to undergo methylation with diazomethane. Prolonged contact in cold methanol, ether, or chloroform gave unchanged starting material contaminated with a colourless substance which, although not obtained pure, did not appear to be either the mono- or di-methyl ether, and presumably arose by reaction with the carbonyl group. Strong hydrogen bonding of the 8-hydroxyl group, demonstrated by the formation of a sparingly alkali-soluble monomethyl ether with methyl sulphate and a monophenylurethane with excess of phenyl *iso*cyanate, would prevent the formation of an 8-methyl ether, but the 5-hydroxyl group should behave in a normal manner. The possibility that the latter might exist in a keto-form such as (VII) was excluded by examination of its infra-red spectrum in the crystalline state and in chloroform solution (carbon tetrachloride could not be used at ordinary temperatures). The results are shown in the table.



(VII)

	Frequency (cm.$^{-1}$)			
		C=O		OH
Solid	1577	1619		3279
Chloroform solution	1590	1619	1644	3590

The band at 1619 cm.$^{-1}$ obtained in solution is actually a " shoulder " on the 1644 cm.$^{-1}$ band and may indicate some aggregation of the solute molecules in the dilute, but saturated, chloroform solution, or it may be due to particles of undissolved material. Both in the solid state and in solution the compound exhibits one carbonyl band and one hydroxyl band which is consistent with (VI; R = H) whereas (VII) would be expected to show two carbonyl bands with the hydroxyl band suppressed. The other bands in the 6μ region at 1577 cm.$^{-1}$ and 1590 cm.$^{-1}$ are assigned to a vibration of the benzene ring.

Experimental

5 : 8-Dihydroxy-1-tetralone.—(*a*) Juglone (1 g.) in ethyl acetate (100 c.c.) was hydrogenated in the presence of Raney nickel. One mol. of hydrogen was absorbed in 15 minutes and the subsequent slow absorption was allowed to proceed for 2—3 days. After filtration and extraction of the catalyst, the solvent was removed under reduced pressure and the residue extracted with boiling light petroleum (b. p. 100—120°; 1 × 100 c.c., 2 × 20 c.c.). *5 : 8-Dihydroxy-*

1-*tetralone* separated when the solution cooled and was recrystallised from the same solvent, forming fine yellow needles (35%), m. p. 184° (Found: C, 67·25; H, 6·65. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·65%). Concentration of the original mother liquor gave a little β-hydrojuglone.

(*b*) 5 : 8-Dimethoxy-1-tetralone (0·34 g.) was added to a molten mixture of aluminium chloride (4 g.) and sodium chloride (1 g.) at 145°. The mixture was heated rapidly to 180°, maintained at that temperature for 3—4 minutes, and allowed to cool. The product was decomposed with ice and hydrochloric acid, and the suspension heated to 90° and then cooled in ice. The precipitate was collected and crystallised from light petroleum forming pale yellow needles (50%), m. p. and mixed m. p. 184°. Both products formed a *diacetate* which crystallised from dilute alcohol in blades, m. p. 177—178° (Found: C, 63·8, H, 5·4; Ac, 34·5. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4; Ac, 32·8%). The p-*nitrophenylhydrazone* separated from aqueous alcohol in orange-brown micro-crystals, m. p. 272° (decomp.) (Found: C, 61·6; H, 5·0; N, 13·2. $C_{16}H_{15}O_4N_3$ requires C, 61·3; H, 4·8; N, 13·4%). The *phenylurethane* was obtained by refluxing a solution of the tetralone (150 mg.) in light petroleum (50 c.c.; b. p. 100—120°) with phenyl *iso*cyanate (0·3 c.c.) and 2 drops of triethylamine for 2 hours; it crystallised in leaflets, m. p. 181° (Found: C, 67·45; H, 5·3; N, 4·9. $C_{17}H_{15}O_4N$ requires C, 67·45; H, 5·15; N, 4·9%), and gave a violet-brown ferric colour.

8-*Hydroxy*-5-*methoxy*-1-*tetralone*.*—(*a*) A solution of 5 : 8-dihydroxy-1-tetralone (160 mg.) in aqueous sodium hydroxide (10 c.c.; 2N) was methylated by gradual addition of methyl sulphate (1 c.c.) with vigorous shaking. The precipitate which formed was collected, washed with water, and crystallised from dilute acetone; it formed pale yellow needles, m. p. 98°. Acidification of the filtrate gave a further quantity of less pure methyl ether. When a larger excess of methyl sulphate was used at 60° the methyl ether remained in solution but the product was less pure.

(*b*) 5 : 8-Dihydroxy-1-tetralone (100 mg.) in acetone (20 c.c.) was refluxed for 2 hours with methyl sulphate (1 c.c.) and anhydrous potassium carbonate (2 g.) and then poured into water (80 c.c.). The solution was warmed to remove most of the acetone and then cooled in ice. The crystalline precipitate was collected and recrystallised from very dilute acetone, forming fine pale yellow needles, m. p. 98° (Found: C, 68·5; H, 6·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%). Repetition of the process with double quantities of methyl sulphate and potassium carbonate for 4 hours did not effect any further methylation nor did methyl iodide under similar conditions. The methyl ether was only slightly soluble in cold dilute sodium hydroxide forming a yellow solution; it gave a prussian-blue colour with ferric chloride.

5 : 8-*Dimethoxy*-1-*tetralone*.—γ-(2 : 5-Dimethoxyphenyl)butyric acid (1·75 g.) (Fieser, Gates, and Kilmer, *J. Amer. Chem. Soc.*, 1940, **62**, 2966) was warmed on a water-bath for 30 minutes with sulphuric acid (3·5 c.c.; 85%), and the solution then cooled and diluted with ice water. The mixture was extracted with ether, and the extract washed with water, dilute ammonia solution, and water, and then dried ($CaSO_4$). Removal of the solvent left a semi-crystalline residue which crystallised from light petroleum (b. p. 30—40°) in micro-needles (25%), m. p. 63° (Found: C, 69·6; H, 6·7. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). The *semicarbazone** formed small needles, m. p. 190° (from aqueous alcohol) (Found: N, 15·9. $C_{13}H_{17}O_3N_3$ requires N, 15·95%). The dimethoxytetralone is soluble in concentrated hydrochloric acid. Cyclisation of γ-(2 : 5-dimethoxyphenyl)butyric acid with anhydrous hydrofluoric acid gave a very poor yield of the tetralone.

1 : 2 : 3 : 4-*Tetrahydro*-1 : 5-*dihydroxy*-4-*ketonaphthalene*.—β-Hydrojuglone (2·21 g.) was hydrogenated in ethyl acetate in the presence of Raney nickel. One mol. of hydrogen was absorbed in 4·5 hours. The light yellow product was extracted repeatedly with boiling hexane (*ca.* 500 c.c. in all) from which the *keto-alcohol* crystallised on cooling. It separated from hexane in needles (68%), m. p. 100° (Found: C, 67·5; H, 5·65. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·65%). The p-*nitrophenylhydrazone* formed dull yellow micro-crystals (from aqueous alcohol), m. p. 222—223° (decomp.) (Found: C, 61·4; H, 4·95; N, 13·2. $C_{16}H_{15}O_4N_3$ requires C, 61·3; H, 4·8; N, 13·4%).

Dehydration of the keto-alcohol. A solution of the keto-alcohol (0·57 g.) in alcohol (10 c.c.) was refluxed for 1 hour with concentrated hydrochloric acid (10 c.c.), and then poured on ice, and the mixture extracted with ether. The extract was dried and evaporated, leaving a semi-solid residue. This was extracted with hot water (charcoal); needles of 1 : 8-dihydroxynaphthalene, m. p. 140°, separated when the extract cooled; the diacetate had m. p. and mixed m. p. with an authentic specimen, 148°.

* Since this paper was submitted these compounds have been described by Cocker, Cross, and McCormick (*J.*, 1952, 72).

5 : 8-*Diacetoxy*-1 : 2 : 3 : 4-*tetrahydro*-1-*keto*-6-*methylnaphthalene*.—The *diacetate* crystallised from water in prismatic needles, m. p. 130° (Found : C, 65·3; H, 5·85; Ac, 32·4. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·85; Ac, 31·2%).

Analyses are by Drs. Weiler and Strauss. The author is indebted to Mr. T. S. Robinson for the infra-red spectra determinations.

MARISCHAL COLLEGE, ABERDEEN. [*Received, January 15th*, 1952.]

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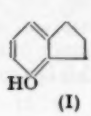
336. *Some Reactions of Indan-4-ol.*

By WILSON BAKER, J. F. W. MCOMIE, and T. L. V. ULBRICHT.

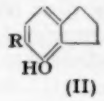
Indan-4-ol reacts in positions 5 and 7 when nitrated and when coupled with diazotised *p*-nitroaniline, and is oxidised by potassium persulphate to indane-4 : 7-diol. The Claisen rearrangement of 4-allyloxyindane gives the 5-allyl derivative, and the Fries rearrangement of 4-acetoxyindane gives a mixture of 5- and 7-acetylindan-4-ol. These hydroxy-ketones are oxidised by hydrogen peroxide in the presence of tetramethylammonium hydroxide and sodium hydroxide respectively to indane-4 : 5- and -4 : 7-diol. 4-Methoxyindane is brominated to 7-bromo-4-methoxyindane.

INDAN-4-OL (I) was first prepared as an oil by Moschner in 1901 (*Ber.*, 1901, **34**, 1257) starting from indane and proceeding *via* indane-4-sulphonic acid (the main product is the 5-sulphonic acid); this synthesis has been improved by Arnold and Zaugg (*J. Amer. Chem. Soc.*, 1941, **63**, 1317). The compound was first obtained crystalline by Goth (*Ber.*, 1928, **61**, 1459), who prepared it from 4-nitroindane (available in 21% yield by low-temperature nitration of indane, Lindner and Bruhin, *Ber.*, 1927, **60**, 435) *via* the amine and diazonium salt, and this method was improved by Lindner, Schmitt, and Zaunbauer (*Monatsh.*, 1939, **72**, 216). Indan-4-ol was isolated from coal tar by Kruber and Schmieden (*Ber.*, 1939, **72**, 653). It is now produced from this source by Coalite and Chemical Products, Limited, of Bolsover, Derbyshire, and we thank Dr. H. F. Bondy for a generous gift of this phenol.

The only recorded substitution reaction of indan-4-ol appears to be its coupling in position 7 with diazotised sulphanilic acid (Arnold and Zaugg, *loc. cit.*), and we now describe a number of its simple reactions.



(I)



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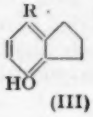

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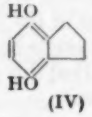

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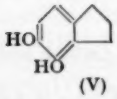

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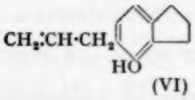

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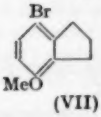

(VII)

Nitration of indan-4-ol (I) in glacial acetic acid gave a 41% yield of 5-nitroindan-4-ol (II; R = NO_2) and an 8% yield of the 7-nitro-compound (III; R = NO_2). Coupling with diazotised *p*-nitroaniline gave a high yield of 7-*p*-nitrophenylazoindan-4-ol (III; R = *p*-NO_2·C_6H_4·N_2) but under 1% of 5-*p*-nitrophenylazoindan-4-ol (II; R = *p*-NO_2·C_6H_4·N_2) isolated by chromatography on alumina; the orientation of these compounds was proved by reduction of the former to 7-aminoindan-4-ol and oxidation of this to the known indane-4 : 7-quinone. Formylation of (I) by the hexamine–acetic acid method (Duff and Bills, *J.*, 1932, 1987; 1934, 1305) gave the dialdehyde, 5 : 7-diformylindan-4-ol. The Elbs

persulphate oxidation (see Baker and Brown, *J.*, 1948, 2303) applied to (I) yielded as the only product indane-4 : 7-diol (IV), characterised by formation of its diacetate and by oxidation with ferric chloride to indane-4 : 7-quinone. This quinone when submitted to Thiele acetylation yielded 4 : 5 : 7-triacetoxyindane. 4-Acetoxyindane, when treated with aluminium chloride, gave a mixture (in varying proportions according to the experimental conditions) of the steam-volatile 5-acetyl-indan-4-ol (II; R = CH_3·CO) and 7-acetyl-indan-4-ol (III; R = CH_3·CO); the latter was oxidised under the usual conditions by alkaline hydrogen peroxide (Dakin oxidation) to indane-4 : 7-diol (IV).

Attempts to oxidise 5-acetylindan-4-ol to indane-4 : 5-diol (V) by hydrogen peroxide in aqueous sodium hydroxide, as in the case of the isomer, did not succeed, probably owing to the very sparing solubility of the alkali salt of the *o*-hydroxy-ketone which may be largely covalent owing to co-ordination with the carbonyl oxygen atom. The difficulty was overcome by using as alkali tetramethylammonium hydroxide, whose salt with the hydroxy-ketone must be ionised, and which readily dissolves 5-acetylindan-4-ol; oxidation in presence of this base proceeded normally, giving indane-4 : 5-diol (V) isolated as its diacetate. Tetramethylammonium hydroxide, or similar quaternary bases such as benzyltrimethyl-ammonium hydroxide, may find useful application in the Dakin oxidation or alkylation with alkyl sulphates of *o*-hydroxy-ketones which give sparingly soluble, possibly co-ordinated alkali salts with sodium and potassium hydroxide.

The Claisen thermal rearrangement of 4-allyloxyindane gave 5-allylindan-4-ol (VI), which shows the properties of a phenol with a free *para*-position.

Indan-4-ol is converted into 7-bromo-4-methoxyindane (VII) by methylation with methyl sulphate and alkali, and then bromination in acetic acid, the overall yield of pure compound being 81%. 4-Halogenoindanes (Barnes and Gordon, *J. Amer. Chem. Soc.*, 1949, **71**, 2644) and especially 7-bromo-4-methoxyindane (VII) (Barnes, Kraft, and Gordon, *J. Amer. Chem. Soc.*, 1949, **71**, 3523) are potentially important intermediates in syntheses of steroids in which rings A and B are built unambiguously on to the 4- and the 5-position of an indane which provides rings C and D. 7-Bromo-4-methoxyindane (VII) has previously been made from *p*-bromophenol and acrylonitrile by a six-step synthesis in an overall yield of 14·3% (Barnes, Kraft, and Gordon, *loc. cit.*).

In all these reactions indan-4-ol behaves as a normal *o*-substituted phenol, and this is in harmony with the preliminary results of Nowlan, Slavin, and Wheeler (*J.*, 1950, 340). The original hypothesis of Mills and Nixon (*J.*, 1930, 2510) predicted that the C–C bond common to the two rings in indanes should be single rather than double in character, and that in consequence bonds C_4–C_5 and C_6–C_7 should behave as single bonds. Considerable evidence, both practical (including the present work) and theoretical (see Springall, Hampson, May, and Spedding, *J.*, 1949, 1524; Berthier and Pullmann, *Bull. Soc. chim.*, 1950, **17**, 88) has, however, accumulated to show that this hypothesis is no longer tenable, and that the departure of the central C–C bond from the character of an ordinary aromatic link towards that of a single bond is extremely slight. The arrangement of the double bonds in formulæ (I)—(VII) of this paper is purely formal, and is not intended to imply that this is a preferred structure.

Experimental

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

5- and 7-Nitroindan-4-ol.—A solution of concentrated nitric acid (1 c.c.; *d* 1·42) in acetic acid (10 c.c.) was added to one of indan-4-ol (2 g.) in acetic acid (10 c.c.). After ½ hour at room temperature the mixture was steam-distilled, and the crystalline *5-nitroindan-4-ol* (1·1 g.) which separated from the distillate was recrystallised from aqueous methanol and obtained as yellow needles, m. p. 56—57° (Found: C, 60·6; H, 5·3; N, 7·8. $C_9H_9O_3N$ requires C, 60·3; H, 5·1; N, 7·8%). This substance gives a red sodium salt, but no ferric chloride reaction.

The residual liquid from the steam-distillation was boiled with charcoal, filtered, and cooled, giving *7-nitroindan-4-ol* (0·2 g.) which, after crystallisation from water, gave pale buff-coloured needles, m. p. 152—153° (Found: C, 60·6; H, 4·9; N, 7·7%). It gives a yellow sodium salt and a negative ferric chloride reaction.

7- *and* **5-p-***Nitrophenylazoindan-4-ol.*—A solution of *p*-nitrobenzenediazonium chloride (1·1 mols.) was added slowly to an ice-cooled solution of indan-4-ol (1·0 mol.) in an excess of 15% aqueous sodium hydroxide, the mixture was then acidified, and the red solid was collected, washed, and dried (yield 90%). It was first crystallised several times from aqueous ethanol, and the two constituents were separated chromatographically on a column of alumina, with ethanol as solvent. Elution readily enabled the small amount of material contained in the more rapidly moving yellow band to be separated from the substance contained in the brown band. The yellow band gave a product in a yield of about 0·25% which, after sublimation, gave 5-p-*nitrophenylazoindan-4-ol* as small reddish-brown needles, m. p. 185° (Found: N, 15·0. $C_{15}H_{13}O_3N_3$ requires N, 14·8%). The brown band yielded a product which, after crystallisation from aqueous ethanol, and then aqueous dioxan gave 7-p-*nitrophenylazoindan-4-ol* as a red, crystalline powder, m. p. 189—190° (decomp.) (Found: C, 63·6; H, 4·7; N, 14·9. $C_{15}H_{13}O_3N_3$ requires C, 63·6; H, 4·6; N, 14·8%). Reduction of the latter azo-derivative at about 45° with sodium dithionite (hydrosulphite) in dilute alcoholic solution in presence of sodium carbonate and final addition of much water precipitated the amphoteric 7-aminoindan-4-ol (Arnold and Zaugg, *loc. cit.*), and oxidation of this with ferric chloride in dilute hydrochloric acid followed by steam-distillation under slightly diminished pressure gave the steam-volatile indane-4 : 7-quinone (see below).

5 : 7-*Diformylindan-4-ol.*—A mixture of indan-4-ol (2·0 g.) and hexamine (2 g.) in acetic acid (8 c.c.) was heated on a boiling-water bath for 6 hours. Concentrated hydrochloric acid (15 c.c.) and water (15 c.c.) were then added and heating continued for ½ hour, after which the mixture was steam-distilled. The crystalline product (0·5 g.) which separated from the distillate (1200 c.c.) was recrystallised twice from methyl alcohol and then sublimed *in vacuo* at 110—120°, giving 5 : 7-*diformylindan-4-ol* as small needles, m. p. 124—125° (Found: C, 69·8; H, 5·2. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). Its alcoholic solution gives a deep reddish-purple colour with ferric chloride. No monoformyl compound, either volatile or involatile in steam, could be isolated, even when the reaction time was reduced to 2 hours.

Indane-4 : 7-diol (IV).—(a) *By the Elbs persulphate oxidation of indan-4-ol.* To a solution of indan-4-ol (3·0 g.; 1 mol.) in 2N-sodium hydroxide (55 c.c.; 5 mols.) was added during 4 hours an aqueous solution of potassium persulphate (5·7 g.; 1 mol.) saturated at room temperature. The temperature of the mixture was not allowed to rise above 20°, and after being left overnight it was saturated with carbon dioxide and extracted with ether to remove indan-4-ol (0·6 g.). The aqueous solution was now made strongly acid with hydrochloric acid, heated on the water-bath for ½ hour, saturated with sodium chloride, and extracted with ethyl acetate. The extract was washed with a little saturated aqueous sodium hydrogen carbonate, and then yielded the crude indane-4 : 7-diol (1·0 g.). It was purified by sublimation at 160—180° *in vacuo*, and then recrystallisation from ethyl methyl ketone–light petroleum (b. p. 60—80°), giving thin, irregular prisms, m. p. 183—184° (Found: C, 71·7; H, 6·7. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%). Arnold and Zaugg (*loc. cit.*) give m. p. 184—185°. 4 : 7-*Diacetoxyindane*, prepared by boiling the dihydroxy-compound with acetic anhydride and a little pyridine for 3 hours and pouring into water, was crystallised several times from methanol and obtained in long needles, m. p. 143—144·5° (Found: C, 66·5; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

(b) *By oxidation of 7-acetylindan-4-ol with hydrogen peroxide.* 7-Acetylindan-4-ol (1·5 g.; 1 mol.; see below) was dissolved in 0·1N-aqueous sodium hydroxide (10 c.c.), and 3% hydrogen peroxide (13 c.c.; 1·25 mols.) added at room temperature. A slow rise in temperature of 14° took place, and after 2 hours a little sodium dithionite (hydrosulphite) was added and the solution was acidified with dilute sulphuric acid, saturated with sodium chloride, and extracted with ethyl acetate. The extract was shaken with saturated aqueous sodium hydrogen carbonate, dried, and evaporated, leaving a crude product (0·8 g.) which was purified as above, giving finally indane-4 : 7-diol (IV), m. p. and mixed m. p. 182—184°.

Indane-4 : 7-quinone.—Indane-4 : 7-diol (1 g.), suspended in water (50 c.c.) and covered with a layer of benzene (50 c.c.), was treated slowly, whilst being shaken, with a solution of ferric chloride (2 g.; anhyd.) in water (20 c.c.) and a few drops of concentrated hydrochloric acid. The mixture was shaken for a further ½ hour, the benzene layer separated, and the aqueous layer extracted several times with benzene. The united benzene solutions yielded a dark red product (0·8 g.) which, after sublimation, was obtained as golden-yellow prisms (0·55 g.), m. p. 42—43°. Arnold and Zaugg (*loc. cit.*) record m. p. 41—42°.

4 : 5 : 7-*Triacetoxyindane.*—Indane-4 : 7-quinone (0·5 g.) was dissolved in acetic anhydride (4 c.c.), and concentrated sulphuric acid (1 drop) added. The mixture was boiled for ¾ hour, poured into water, and extracted with ether, and the extract washed with aqueous sodium hydrogen

carbonate, then with 1% aqueous sodium hydroxide, dried, and distilled. After several crystallisations from benzene–light petroleum (b. p. 60—80°) **4 : 5 : 7-*triacetoxyindane*** was obtained in small prisms, m. p. 92—93° (Found : C, 61·4; H, 5·4. $C_{15}H_{16}O_6$ requires C, 61·6; H, 5·5%).

4-*Acetoxyindane*.—A solution of indan-4-ol (4·5 g.; 1 mol.) in one of sodium hydroxide (2·0 g.; 1·1 mols.) in water (15 c.c.) containing crushed ice was vigorously shaken after the addition of acetic anhydride (4·2 c.c.; 1·3 mols.), and the solid product collected, washed, and dried (yield 5·6 g.). A portion, after crystallisation from aqueous methanol, was obtained as prisms, m. p. 31—32° (Lindner, Schmitt, and Zaunbauer, *Monatsh.*, 1939, **72**, 216, give m. p. 30—32°).

5- *and* 7-*Acetylindan*-4-*ol*.—4-Acetoxyindane (5·0 g.; 1 mol.) was melted, anhydrous aluminium chloride (5·6 g.; 1·2 mols.) added, and the mixture heated on the steam-bath for 5 hours, and submitted to steam-distillation after addition of dilute hydrochloric acid. The solid **5-*acetylindan*-4-*ol*** in the distillate (1200 c.c.) was collected (yield : 3·0 g., 60%) and recrystallised from aqueous ethanol, being obtained in small plates, m. p. 47° (Found : C, 74·7; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%). It forms a yellow, very sparingly soluble sodium salt, and its alcoholic solution gives a strong, purple ferric chloride reaction. The residue from the steam-distillation was cooled, the solid collected (1·6 g., 32%), recrystallised from methanol, and finally sublimed (at 170—180°/30 mm.), giving **7-*acetylindan*-4-*ol*** as prismatic needles, m. p. 185° (Found : C, 75·3; H, 7·1%). It gives a weak yellow colour with ferric chloride in ethanol solution.

The yields of 5- and of 7-acetylindan-4-ol when the Fries reaction was carried out at 140—150° (3 hours) were 57 and 20% respectively, and when nitrobenzene was used as solvent at room temperature (48 hours) the yields were 22 and 48% respectively.

Oxidation of **5-*Acetylindan*-4-*ol* *with Hydrogen Peroxide in Presence of Tetramethylammonium Hydroxide.*** **4 : 5-*Diacetoxyindane*.**—5-Acetylindan-4-ol (1·5 g.; 1 mol.) was dissolved in a 10% aqueous solution of tetramethylammonium hydroxide (20 c.c.; 2·5 mols.) at room temperature, and a 6% aqueous solution of hydrogen peroxide (6·5 c.c.; 1·25 mols.) added in an atmosphere of nitrogen. A spontaneous rise in temperature to 40° occurred during 10 minutes; after ½ hour the mixture was warmed again to 40°, and after a further 20 minutes a little sodium dithionite (hydrosulphite) was added to the cooled solution, which was then acidified with dilute sulphuric acid and extracted thoroughly with ether–ethyl acetate. The extracts were shaken with 2% aqueous sodium hydroxide, the alkaline layer was acidified and again extracted as before, and the extracts were distilled, leaving a semi-solid product (0·4 g.). This was boiled with acetic anhydride (2 c.c.) and a trace of sulphuric acid for 1 hour, then shaken with water, and the dark oil heated (at 80—100°/20 mm.), giving a sublimate (45 mg.), m. p. 72—74°. Crystallisation from aqueous ethanol and final sublimation gave **4 : 5-*diacetoxyindane*** as prisms, m. p. 79—80° (Found : C, 66·3; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

4-*Allyloxyindane*.—A mixture of indan-4-ol (2 g.), allyl iodide (2·7 g.), ethyl methyl ketone (35 c.c.), and anhydrous potassium carbonate (2·4 g.) was boiled for 24 hours, then poured into water, and the oily *product* isolated and distilled, giving a pale yellow liquid (2·1 g.), b. p. 122—125°/14 mm. (Found, in material twice distilled : C, 82·6; H, 8·2. $C_{12}H_{14}O$ requires C, 82·7; H, 8·1%).

5-*Allylindan*-4-*ol* (VI).—4-Allyloxyindane (3·6 g.) was heated in an oil-bath at 220° for 2 hours, and the product dissolved in ether and repeatedly extracted with small quantities of 2N-sodium hydroxide. The united alkaline extracts were acidified and yielded to ether an oil, b. p. 101—102°/0·7—0·8 mm. (2·1 g.) (Found, in material redistilled at 0·2 mm. : C, 82·6; H, 8·0. $C_{12}H_{14}O$ requires C, 82·7; H, 8·1%). This **5-*allylindan*-4-*ol*** dissolves only slightly in dilute aqueous sodium hydroxide, and gives virtually no colour with ferric chloride in alcoholic solution. It gives a blue indophenol reaction with *p*-aminodimethylaniline and alkaline hypochlorite, and a purplish-blue colour with alkaline 2 : 6-dichloroquinonechloroimide (see Gibbs, *J. Biol. Chem.*, 1927, **72**, 649), reactions indicative of a phenol with a free *para*-position. When heated with α-naphthyl *iso*cyanate and a trace of triethylamine it gave the related α-naphthylurethane, which was crystallised from light petroleum; it is probably dimorphic and melted at 70—80° depending on the rate of heating, and after cooling and reheating it then melted at 126—128°.

7-*Bromo*-4-*methoxyindane* (VII).—Indan-4-ol (10 g.), dissolved in a little dilute sodium hydroxide, was shaken vigorously during the portionwise addition of sodium hydroxide (20 g.) in water (75 c.c.) and methyl sulphate (30 g.), the temperature being kept at about 50°. After 2 hours' heating on the water-bath, the mixture was diluted, and then yielded to ether 4-methoxyindane as an oil (10·2 g.). To this crude product in glacial acetic acid (20 c.c.) was added drop-

wise, whilst cooling in water, a solution of bromine (11·1 g.; 1 mol.) in acetic acid (20 c.c.), and the mixture was then vigorously shaken with water (100 c.c.). The oil rapidly crystallised, and was collected, washed, and dried (yield 15·5 g.; m. p. 60—63°). Recrystallisation from light petroleum (b. p. 40—60°) gave 4 crops (totalling 13·8 g.; 81% from indan-4-ol), m. p. 66° (Barnes, Kraft, and Gordon, *loc. cit.*, give m. p. 66—66·5°).

THE UNIVERSITY, BRISTOL. [*Received, January 17th*, 1952.]

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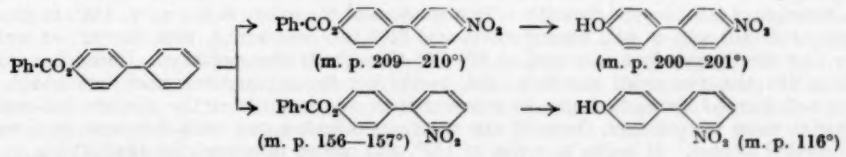
337. *The Nitration of Esters of 4-Hydroxydiphenyl. The Preparation of 4-Hydroxy-4′- and -2′-nitrodiphenyls.*

By BRYNMOR JONES and (in part) FRANK CHAPMAN.

Investigations into the preparation of 4-hydroxy-4′-nitrodiphenyl from 4-hydroxydiphenyl have led to an examination of the nitration in acetic acid solution of the benzoate, benzenesulphonate, toluene-*p*-sulphonate, and acetate of 4-hydroxydiphenyl. It has been established that nitration does not occur exclusively in the 4′-position, but that substantial amounts of the 2′-nitro-esters are formed. An improved method of preparing 4-hydroxy-4′-nitrodiphenyl from the benzoate is described.

ALTHOUGH the literature records a number of investigations of the halogenation of esters of 4-hydroxydiphenyl, their behaviour on nitration has been but little studied. Such information as there is suggests that a single product is formed, and that substitution takes place in the 4′-position. For instance, in the nitration of the toluene-*p*-sulphonate, Bell and Kenyon (*J.*, 1926, 3046) obtained 4′-nitro-4-diphenylyl toluene-*p*-sulphonate. No yield was recorded, but substitution was believed to occur mainly, if not exclusively, in the 4′-position (cf. Waters, " Physical Aspects of Organic Chemistry," 1950, p. 504, where this behaviour is erroneously attributed to the acetate). Later, Hazlet and van Orden (*J. Amer. Chem. Soc.*, 1942, **64**, 2505) nitrated the benzoate and obtained a 40% yield of the unpurified 4′-nitro-4-diphenylyl benzoate. Although this material required several crystallisations before purification was achieved, no other product was isolated, and nitration was stated categorically to occur in one position only. Such a conclusion is at variance with the extensive studies by Le Fèvre and Turner (*J.*, 1928, 247; see Turner, *Rec. Trav. chim.*, 1929, **48**, 821) and by Bell and Kenyon (*J.*, 1926, 2705) on substitution in diphenyl and its derivatives, for not only is the phenyl group itself *op*-directing, but it remains so even when it contains a powerful deactivating substituent, such as a nitro-group.

A careful re-examination of the nitration of the benzoate in acetic acid, in which more precise conditions for the reaction have been worked out, has shown the product to be a mixture of the 4′-nitro- and the 2′-nitro-isomer. A strictly quantitative analysis of the mixture has not been attempted, but it is clear that the 2′-nitro-4-diphenylyl benzoate constitutes at least 25% of the product of nitration. [From 60 g. of the 4-diphenylyl benzoate in two experiments, 31 g. of the 4′- and 17 g. of the 2′-nitro-ester were obtained as pure crystalline products.]



The orientation of this second compound was established by hydrolysis to 4-hydroxy-2′-nitrodiphenyl, followed by oxidation to *o*-nitrobenzoic acid. Its isolation in quantity, together with the principal product, 4′-nitro-4-diphenylyl benzoate, provides a further

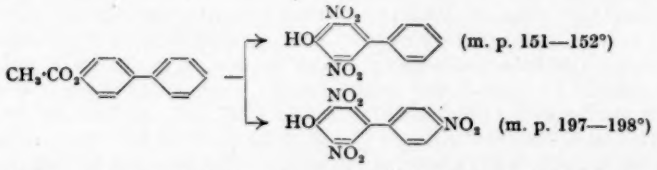
illustration of the *op*-directing influence of a phenyl group containing a deactivating substituent. Benzoylation of the hydroxy-group so reduces its activating influence on the phenyl group to which it is attached that substitution occurs in the other phenyl group.

The benzene- and toluene-*p*-sulphonates behave similarly, but in these cases the reactions were studied less fully because of the greater difficulty in achieving a clean separation of the products of nitration, and also because the primary objective of this investigation was to find a convenient method of preparing 4-hydroxy-4′-nitrodiphenyl. These three esters of 4-hydroxydiphenyl have a low solubility in cold acetic acid and, since their reactivity towards an electrophilic reagent is also low, nitrations are best carried out at 75—90°. At these temperatures nitration proceeds smoothly, without any noticeable hydrolysis or oxidation.

The benzoate is the least soluble, and its nitration differs from that of the sulphonyl esters in that the main product, 4′-nitro-4-diphenylyl benzoate, is so little soluble that it begins to separate from the hot nitrating mixture. The material which finally crystallised from the cold reaction mixture contained some 2′-nitro-ester, but the greater part of this remained in solution.

The products of nitration of the two sulphonyl esters were more soluble in the mixture of acetic and nitric acids, and separation was accomplished less readily. In the case of the toluene-*p*-sulphonate a substantial part of the 4′-nitro-4-diphenylyl toluene-*p*-sulphonate was obtained when the reaction mixture had been kept in ice for several hours. This ester was comparatively free from the 2′-nitro-isomer. The mixture of nitro-esters formed during nitration of the benzenesulphonate proved even more intractable. No solid separated, and the product obtained after dilution had to be subjected to several fractional crystallisations before the 4′- and the 2′-nitro-ester were obtained pure.

The nitration of 4-diphenylyl acetate, even at 40°, by means of either 98% or 70% nitric acid, was accompanied by hydrolysis, and the product in both cases was a mixture containing 4-hydroxy-di- and -tri-nitrodiphenyls. Two constituents were eventually isolated, and these were shown to be 4-hydroxy-3 : 5-dinitro- and -3 : 5 : 4′-trinitrodiphenyl. The mixture may have contained other hydroxynitrodiphenyls, but their presence was not investigated.



These experiments show that the acetate is not a suitable material for the preparation of 4-hydroxy-4′-nitrodiphenyl, and that the nitration of the two sulphonyl esters gives mixtures of isomers which are obtained pure only with difficulty. On the other hand, nitration of the benzoate provides a reliable and convenient method of preparing 4-hydroxy-2′- and -4′-nitrodiphenyls.

Experimental

(M. p.s are uncorrected. The microanalyses were carried out by Drs. Weiler and Strauss Oxford.)

Nitration of 4-Diphenylyl Benzoate.—To a solution of the ester (40 g.; m. p. 148°) in glacial acetic acid (310 ml.) at 85°, fuming nitric acid (100 ml.) was added, with stirring, at such a rate that the temperature was kept at 85—90° throughout the operation. Under these conditions nitration proceeded smoothly, and, as the last few ml. of nitric acid were added, 4′-nitro-4-diphenylyl benzoate began to separate from solution. After the mixture had cooled slowly to room temperature, the solid deposited was collected, and washed in turn with water and methyl alcohol. It began to soften at 155°, and melted completely at 195° (31·5 g.). At this stage the 4′-nitro-4-diphenylyl benzoate was contaminated with some 2′-nitro-ester, but this was readily removed by a single crystallisation from acetic acid (550 ml.), followed by digestion of the resulting solid with boiling acetic acid (200 ml.). When the solution cooled, pure

4′-nitro-4-diphenylyl benzoate (21 g.), m. p. 209—210°, was obtained. The yield of purified 4′-nitro-ester thus obtained was very consistent, despite the fact that the amount of 2′-nitro-ester which separated with it from the reaction mixture varied appreciably in different experiments. For example, in one experiment 20 g. of 4-diphenylyl benzoate gave only 13·6 g. of unpurified 4′-nitro-4-diphenylyl benzoate, but this on crystallisation yielded 10·5 g. of pure material.

From the acetic acid used to purify the 4′-nitro-4-diphenylyl benzoate some 2′-nitro-4-diphenylyl benzoate was isolated by dilution with water. The main crop, however, was obtained from the acetic acid–nitric mother-liquors by dilution. The material obtained from these two sources was often combined, and purified by crystallisation from acetic acid and alcohol.

In some experiments a small crop of substantially pure 2′-nitro-4-diphenylyl benzoate was obtained by keeping the original mother-liquor for several hours before dilution. In an experiment in which 20 g. of 4-diphenylyl benzoate had been used, and from which the 4′-nitro-4-diphenylyl benzoate had been collected, 2·7 g. of an almost pure *2′-nitro-4-diphenylyl benzoate* were obtained (Found: C, 70·1; H, 4·2; N, 4·5. $C_{19}H_{13}O_4N$ requires C, 70·1; H, 4·1; N, 4·4%).

In other experiments the original reaction mixture of acetic and nitric acid was not allowed to cool to room temperature. Instead, it was cooled to 45—50°, and the 4′-nitro-4-diphenylyl benzoate was then collected. Whichever procedure was adopted, about 11 g. of 2′-nitro-4-diphenylyl benzoate were obtained from 40 g. of 4-diphenylyl benzoate, and with reasonable care it was possible to obtain the two nitro-esters in pure forms in yields which together were 70% of the theoretical.

Attempts to prepare 4′-nitro-4-diphenylyl benzoate, following the rather indefinite instructions given by Hazlet and van Orden (*loc. cit.*), failed: the 4-diphenylyl benzoate was invariably recovered unchanged.

*Nitration of 4-Diphenylyl Toluene-*p*-sulphonate.*—The ester (10 g.), dissolved in glacial acetic acid (75 ml.), was nitrated at 90—95° by gradual addition of nitric acid (98%; 15 ml.). After all the acid had been added, the mixture was stirred for an hour. Unlike the nitration of the benzoate, this reaction did not lead to the immediate separation of any product, but during several hours in a refrigerator some 4′-nitro-4-diphenylyl toluene-*p*-sulphonate (4 g.), m. p. 149—152°, separated from solution. This on crystallisation from benzene–ligroin, and from alcohol, gave 3·7 g. of the pure compound, m. p. 156—157° (Bell and Kenyon, *loc. cit.*, record m. p. 156—158°).

Dilution of the nitric acid–acetic acid mother-liquor with water (100 ml.) gave 2′-nitro-4-diphenylyl toluene-*p*-sulphonate as a thick oil which, after solidifying, was dried and crystallised from benzene–ligroin to give 3·5 g. of a product of m. p. 52—56°. Further purification showed this specimen to contain more than 0·5 g. of the less soluble 4′-nitro-ester (m. p. 156°). This fraction was most easily separated by dissolving the more soluble 2′-nitro-ester in boiling methyl alcohol and decanting the clear liquid, which gave *2′-nitro-4-diphenylyl toluene-*p*-sulphonate* (2 g.) as pale yellow prisms, m. p. 79° (Found: C, 62·1; H, 4·0. $C_{19}H_{15}O_5NS$ requires C, 61·8; H, 4·1%). Further crystallisation from methyl alcohol, ligroin, and acetic acid left the m. p. unchanged.

Nitration of 4-Diphenylyl Benzenesulphonate.—To a solution of the ester (20 g.) in glacial acetic acid (35 ml.) at 90°, fuming nitric acid (35 ml.) was added dropwise at such a rate that the temperature was kept at 85—90°. After all the acid had been added, stirring was continued for an hour, and the solution was then set aside for several hours. When the addition of some 4′-nitro-4-diphenylyl benzenesulphonate failed to induce crystallisation, water (15 ml.) was added, and a dark oil was obtained. This eventually hardened to a solid which after crystallisation from alcohol melted over the range 81—90°. Several crystallisations from acetic acid, and from methyl and ethyl alcohol, were needed before 4′-nitro-4-diphenylyl benzenesulphonate was obtained as pale yellow lustrous plates, m. p. 107°. (The identity of this compound was established by mixed m. p. determination with a specimen of the ester prepared from benzenesulphonyl chloride and 4-hydroxy-4′-nitrodiphenyl in pyridine.) Addition of a further volume of water (25 ml.) to the original reaction mixture yielded a second batch of liquid, which also solidified on storage. This, after three crystallisations from alcohol, gave *2′-nitro-4-diphenylyl benzenesulphonate* as pale yellow lustrous plates, m. p. 106° (Found: C, 61·5; H, 3·6. $C_{18}H_{13}O_5NS$ requires C, 60·9; H, 3·7%).

Because the products of nitration were first obtained as oils, their separation and purification were accompanied by substantial losses. Nevertheless, it was possible to isolate several grams of each of the two isomers in pure form. In view of the similarity of the m. p.s and of the crystalline

forms, particular care was taken to establish their identity. On hydrolysis they gave 4-hydroxy-4′- and -2′-nitrodiphenyls.

Nitration of 4-Diphenylyl Acetate.—The acetate was prepared by Hazlet and Kornberg's method (*J. Amer. Chem. Soc.*, 1939, **61**, 3037). The following experiment is typical of several carried out in an attempt to nitrate it.

The acetate (20 g.; m. p. 87°) was dissolved in glacial acetic acid (100 ml.) at 40°, and nitric acid (70%; 40 ml.) was added at such a rate that the temperature was kept at this value. After all the acid had been added, the solution was kept at 40° for a further 30 minutes. In some experiments the product, a mixture of hydroxy-di- and -tri-nitrodiphenyls (19·5 g.; m. p. 143—152°) separated from the warm solution. In others, the product was obtained on cooling (98% nitric acid gave the same product).

From this mixture two hydroxynitrodiphenyls were finally isolated in pure form: the 3 : 5-dinitro-, m. p. 151—152°, and the 3 : 5 : 4′-trinitro-compound, m. p. 197—198°. No easy method of separation was found and, as a result of losses during purification, no estimate can be made of the amount of these two compounds in the original mixture.

A first rough separation was achieved by treating the dry mixture with boiling chloroform, which dissolved the more soluble dinitro-compound, leaving the greater part of the 3 : 5 : 4′-trinitro-compound. This, after many crystallisations from glacial acetic acid, was obtained as pale yellow needles, m. p. 197—198° (Found: C, 47·5; H, 2·5; N, 13·4. Calc. for $C_{12}H_7O_7N_3$: C, 47·1; H, 2·3; N, 13·8%). Evaporation of the chloroform extract gave a product, m. p. 136—140°, which, after crystallisation from acetic acid, gave eventually 4-hydroxy-3 : 5-dinitrodiphenyl as pale yellow plates, m. p. 151—152° (Found: C, 55·6; H, 3·1; N, 11·2. Calc. for $C_{12}H_8O_5N_2$: C, 55·4; H, 3·1; N, 10·8%). The m. p.s of these two compounds were not depressed on their admixture with pure specimens of the compounds prepared respectively by careful nitration of 4-hydroxy-4′-nitrodiphenyl and 4-hydroxydiphenyl.

Hydrolysis of 4′-Nitro- and 2′-Nitro-4-diphenylyl Benzoate.—A suspension of the 4′-nitro-ester (30 g.) in ethyl alcohol (150 ml.) was heated under reflux and hydrolysed by careful addition of a solution of potassium hydroxide (20 g. in 50 ml. of water). The immediate deep red coloration showed that hydrolysis was rapid, but, to ensure that it was complete, the mixture was heated for 15 minutes. On cooling, the potassium salt of 4-hydroxy-4′-nitrodiphenyl separated in deep blue lustrous plates (24 g.). These were dissolved in the minimum volume of hot water and acidified, 4-hydroxy-4′-nitrodiphenyl being precipitated as a bright yellow solid, m. p. 200—201° (18 g.) (Bell and Kenyon, *loc. cit.*, gave m. p. 203°). It gave a methyl ether, m. p. 111°.

2′-Nitro-4-diphenylyl benzoate (15 g.), dissolved in alcohol–acetone (150 ml.), was hydrolysed in a similar manner, but in this case the potassium salt of 4-hydroxy-2′-nitrodiphenyl was not deposited, and on acidification benzoic acid was precipitated. When this had been collected, the filtrate was diluted with water (500 ml.) and a brown oil separated. After several hours, this solidified and, after being dried, it was crystallised from ether–ligroin (b. p. 40—60°). Further crystallisation from carbon tetrachloride gave the 4-hydroxy-2′-nitrodiphenyl as elongated prisms (2·1 g.), m. p. 116° (Found: N, 6·4. Calc. for $C_{12}H_9O_3N$: N, 6·5%). Its methyl ether, m. p. 64°, crystallised from methyl alcohol in the same form.

To a portion of 4-hydroxy-2′-nitrodiphenyl dissolved in aqueous alkali at 40° was added a solution of potassium permanganate until no further decolorisation occurred. The mixture was then heated on a water-bath for an hour. The cold solution was decolorised with sulphur dioxide, and extracted with ether. After removal of the ether, the solid remaining was crystallised from water and gave *o*-nitrobenzoic acid, m. p. 143° (unchanged when the sample was mixed with an authentic specimen).

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UNIVERSITY COLLEGE, HULL.
THE UNIVERSITY, SHEFFIELD.

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338. *The Structure of Alginic Acid. Part II.**

By S. K. Chanda, E. L. Hirst, (the late) E. G. V. Percival, and A. G. Ross.

The methyl derivative of alginic acid has been hydrolysed with formic acid. The products were converted into the methyl esters of methylated methylmannuronoside by means of methanolic hydrogen chloride and diazomethane, and lithium aluminium hydride then yielded the corresponding methylmannosides. The methylated mannoses were separated chromatographically, 2 : 3-dimethyl mannose, identified by oxidation to a derivative of *meso*dimethoxysuccinic acid with periodic acid, being the main component. Traces of 2 : 3 : 4-trimethyl mannose, monomethyl mannose, and dimethyl glucose were also present. The results confirm the view that the main structural feature of the alginic acid molecule is a chain of 1 : 4-linked β-D-mannuronic acid residues, the chain length of the alginic acid used in these experiments being *ca.* 100.

Alginic acid is found, usually as a salt, in certain seaweeds and is readily isolated by soaking the dried and finely ground seaweed in dilute acid, after which the alginic acid can be extracted with aqueous sodium carbonate. The acid itself is insoluble in water but its sodium salt forms highly viscous solutions. The viscosity of these solutions varies greatly from sample to sample and the differences are thought to be due to the varying chain length of the polysaccharide.

Alginic acid has been shown to contain D-mannuronic acid residues (Nelson and Cretcher, *J. Amer. Chem. Soc.*, 1929, **51**, 1914; 1932, **54**, 3409; Bird and Haas, *Biochem. J.*, 1931, **25**, 403), although direct hydrolysis results in very poor yields. More recently Hirst, Jones, and Jones (*J.*, 1939, 1880) prepared a degraded alginic acid by treatment with methylalcoholic hydrogen chloride and methylated it by the thallium method. Hydrolysis of the methylated derivative was difficult but nitric acid caused simultaneous hydrolysis and oxidative degradation to *meso*dimethoxysuccinic acid, indicating that the methyl groups were attached either to $C_{(2)}$ and $C_{(3)}$ or to $C_{(4)}$ and $C_{(5)}$. Proof that the methyl groups were at $C_{(2)}$ and $C_{(3)}$ was obtained by treatment of the methylated alginic acid with methylalcoholic hydrogen chloride, which gave the methyl ester of 2 : 3-dimethyl methyl-D-mannuronoside. These results have been confirmed by the present investigation which was undertaken with the idea of working with a less degraded sample of alginic acid and thereby obtaining information concerning the structure of a larger portion of the alginic acid molecule.

Alginic acid was prepared from *Laminaria digitata* fronds and directly methylated in an atmosphere of nitrogen by methyl sulphate and aqueous potassium hydroxide at room temperature. After sixteen treatments the product had a methoxyl content of 25·8% (yield, 90%). The methylated material was converted into the methyl ester, and viscosity determinations were carried out. If the validity of the Staudinger hypothesis and the applicability of the constant for methylated cellulose used in the calculation can be assumed, the results indicated a molecular weight of about 3000 (Staudinger and Reinecke, *Annalen*, 1938, **535**, 47) but this figure may be much too low.

Hydrolysis of the potassium salt of methylated alginic acid was achieved by using 98% formic acid. Chromatographic investigation of the resulting mixture of methylated mannuronic acids was unsatisfactory owing to trailing, and no convenient spray could be found. In view of this difficulty the mixture was heated with methanolic hydrogen chloride, and the solution was neutralised with diazomethane. The mixed methylated methylmannurosides so obtained were reduced by lithium aluminium hydride (method of Lythgoe and Trippett, *J.*, 1950, 1983) to the corresponding mannoside derivatives, which were readily separated on a cellulose column after aqueous hydrolysis to the methyl mannoses. This hydrolysis was incomplete, as shown by the presence of methylmannosides in the fractions from the

* Part I, *J.*, 1939, 1880.

column. The following fractions were obtained : Fraction (*a*) was a mixture of 2 : 3 : 4-trimethyl mannose with 2 : 3-dimethyl methylmannoside, containing 6·85% of the trimethyl sugar as calculated from the reducing power to alkaline hypoiodite solution. This fraction, on two subsequent hydrolyses, was shown chromatographically to yield only 2 : 3 : 4-tri- and 2 : 3-di-methyl mannoses, the amount of trimethyl mannose being equivalent to 0·98% of the total hydrolysate obtained from the methylated alginic acid. The presence of 2 : 3 : 4-trimethyl mannose was confirmed by demethylation, and by periodate oxidation, after chromatographic separation. Demethylation was achieved by treatment in a sealed tube with concentrated hydrobromic acid (Hough, Jones, and Wadman, *J.*, 1950, 1702) and chromatographic examination of the resulting sugars. No free sugar other than mannose was detected. Oxidation with aqueous periodic acid for twenty hours was carried out and the solution after addition of potassium chloride was decanted. This solution, on addition of solutions of phenylhydrazine hydrochloride and potassium ferricyanide, gave the characteristic port wine colour due to formaldehyde, indicating that no methyl group was present on $C_{(6)}$. Two small fractions (*b*) and (*c*) consisted of di- and mono-methyl methylmannosides respectively. Fraction (*d*) was a dimethyl sugar, later identified as a glucose derivative. Fraction (*e*) was a mixture of the preceding and following fractions. Fraction (*f*) was composed of 2 : 3-dimethyl mannose, identified as the corresponding lactone and by its oxidation to *meso*dimethoxysuccinic acid; this was the main fraction. Fraction (*g*) was small, consisting of monomethyl mannose. Analysis of the various fractions indicated that the hydrolysate had the following percentage composition : 2 : 3 : 4-trimethyl mannose, 1; dimethyl glucose, 6; 2 : 3-dimethyl mannose, 88; monomethyl mannose, 4·5.

These results coupled with the high yields obtained at each stage and with the high negative rotations of derivatives of the alginic acid confirm the view that alginic acid is composed mainly, or perhaps entirely, of β-D-mannuronic acid residues linked between $C_{(1)}$ and $C_{(4)}$. The origin of the dimethyl glucose mentioned above is as yet unexplained. It was thought that it might be due to epimerisation in the alkaline conditions of the reduction with lithium aluminium hydride, but a control experiment on 2 : 3-dimethyl mannose negatived this possibility and indicated merely that a small degree of demethylation took place which might account for much of the monomethyl mannose found in the present series of experiments. Further work will be necessary to decide whether the glucose is due to impurity or originates from some part of the structure of alginic acid.

The proportion of trimethyl mannuronic acid in the products of hydrolysis indicates the presence of one end group for every hundred mannuronic acid residues. This particular sample of alginic acid appears therefore to have a chain length of about 100. The viscosity of this sample was comparatively low and further investigations are clearly desirable with alginic acid of high viscosity as starting material, but the experimental difficulties will be extremely formidable. The present results are nevertheless of value in that they show that the type of structure previously proved only for highly degraded alginic acid may be extended to alginic acids of much higher molecular weight.

Experimental

Methylation of Alginic Acid.—The sample was prepared from *Laminaria digitata* fronds in the Institute of Seaweed Research Laboratory by soaking the dried ground weed overnight in 0·2N-acid, followed by extraction with sodium carbonate solution (3%). The alginic acid (purity 98%) was recovered by conversion into the calcium salt and treatment of the latter with 2N-hydrochloric acid, followed by separation, washing, and drying. Alginic acid (40 g.) was dissolved in aqueous potassium hydroxide (50%; 900 c.c.), and methyl sulphate (450 c.c.) was added with vigorous stirring during 5 days, in an atmosphere of nitrogen at room temperature. The solution was treated with further alkali (300 c.c.) and methyl sulphate (150 c.c.), dialysed, and concentrated *in vacuo* at 35°/15 mm., giving methylated potassium alginate. After four methylations the product had OMe, 11·8%. After sixteen methylations the methoxyl content was 25·8% (Calc. for $C_9H_{11}O_6K$: OMe, 25·6%). The yield was 50 g., and $[\alpha]_D^{15}$ −118° (*c*, 1·0 in water).

Preparation of the Methyl Ester.—The potassium salt (20 g.) was dissolved in water (200 c.c.) and treated with ten times the amount of hydrochloric acid required to form the free acid, and

the solution was dialysed until free from chloride ions, neutralised with silver oxide, and centrifuged. The silver salt was obtained by precipitation with acetone, separated, and dried. Attempts to convert this salt into the methyl ester by (*a*) boiling methyl iodide and silver oxide and (*b*) treatment with methanolic hydrogen chloride and diazomethane were unsuccessful. More success was achieved by the following method. The silver salt (5 g.) was dissolved in water (1 l.), and 2N-nitric acid added (400 c.c.). The solution was then dialysed for 3 days. Further nitric acid (100 c.c.) was added and dialysis continued for 7 days, whereafter the solution was treated with Amberlite I.R. 100 resin for 5 days and then concentrated in the presence of silver oxide. The residue was heated under reflux for 3 days with methyl iodide (200 c.c.), and the solution was then diluted with methanol, centrifuged, and evaporated to dryness. The solid residue was treated with methanolic hydrogen chloride (1%; 25 c.c.) for 12 hours at 0°, then neutralised with ethereal diazomethane, and the solution was evaporated to dryness. The last-mentioned treatment was repeated and the residue was extracted with chloroform which was evaporated to a thin syrup and poured into light petroleum (b. p. 60—80°), giving a precipitate which was separated and dried (2·5 g.) (Found: OMe, 41·8. Calc. for $C_9H_{14}O_6$: OMe, 42·6%). The product had $[\alpha]_D^{15}$ −87° (*c*, 8·0 in chloroform), −126° (*c*, 0·9 in *m*-cresol), $\gamma_{sp.}^{20}/c$, 3·9 (*c*, 0·9 in *m*-cresol).

Hydrolysis of Dimethyl Potassium Alginate.—A solution of the polysaccharide (5 g.) in formic acid (500 c.c.; 98%) to which some charcoal was added was heated on a water bath. $[\alpha]_D^{15}$ changed from −118° to +14° in 8 hours. The solution was concentrated *in vacuo* to a syrup which was dissolved in water (200 c.c.). The solution was heated on a boiling-water bath for 4 hours, and concentrated to a syrup. Dissolution in water and concentration were repeated several times to remove traces of formic acid. Potassium ions were removed by treatment in water with Amberlite I.R. 100 resin overnight, the resin removed by filtration, and the solution concentrated to a syrup which was extracted with acetone. Evaporation of the solvent yielded a glassy solid (4·2 g.).

This material was examined chromatographically with *n*-butanol–acetic acid–water (4 : 1 : 5) as solvent and aniline oxalate as spray. Three spots were identified with R_G values, 0·65, 0·59, and 0·46, respectively, but the last spot which represented the bulk of the material showed a long trail almost to the starting line. An attempt to separate the mixture on a cellulose column with *n*-butanol–acetic acid (4 : 1) partly saturated with water was unsatisfactory. Various other solvent mixtures of different proportions of butanol, light petroleum, and acetic acid were tried without success.

Conversion into Ester before Separation.—As the trailing on the paper chromatogram was thought to be due to lactonisation and that this might be avoided by esterification, methylated alginic acid was dissolved in acetone–methanol (10 : 1), and the solution cooled in ice–salt and neutralised with diazomethane. The solution was left in the refrigerator in the presence of excess of diazomethane and then concentrated to a thin syrup. Examination of this syrup on the chromatogram showed improved definition of the spots but these were very faint and close together. Various spraying agents were tried without great success, the most satisfactory being aqueous aniline oxalate and dimethyl-*p*-phenylenediamine in trichloroacetic acid.

Reduction with Lithium Aluminium Hydride.—The potassium salt of methylated alginic acid (3·81 g.) was hydrolysed with formic acid as described previously, and the metallic ions were removed by two treatments with Amberlite I.R. 100 resin, the mixture of methylated mannuronic acids being finally obtained as a syrup (1·46 g.). The syrup was boiled with methanolic hydrogen chloride (50 c.c.; 1%) for 7 hours and the solution neutralised with diazomethane and concentrated *in vacuo* to a brown glass (1·47 g.). The glass was treated with gently boiling dry ethereal lithium aluminium hydride (2—3 g. in 50 c.c.) for 4 hours; then, after cooling, the excess of reagent was carefully destroyed with water, and the whole acidified with sulphuric acid (2N) and neutralised with barium carbonate. Aluminium was precipitated as the hydroxide by barium hydroxide, and barium and lithium were removed as carbonates (carbon dioxide), and the clear solution after filtration was concentrated *in vacuo*, giving a solid residue which was extracted with boiling chloroform. This yielded a syrup, which (2·90 g.) was converted into the methyl glycoside-ester and treated again as above to ensure complete reduction to mannose derivatives. The chloroform-insoluble solid was treated in the same way, giving a total yield of 2·70 g. The methylmannosides were hydrolysed with 2N-sulphuric acid (75 c.c.; 5·5 hours), and the free sugars (2·08 g.) were isolated in the usual way.

Chromatographic Analysis.—Paper chromatographic analysis of the above free sugars showed the presence of trimethyl mannose, R_G 0·75 (weak), dimethyl mannose, R_G 0·54 (very strong), and monomethyl mannose, R_G 0·34 (weak).

The main bulk of the syrup (2·08 g.) was separated on a cellulose column (90 × 3 cm.) (Hough, Jones, and Wadman, *J.*, 1949, 2511), with light petroleum (b. p. 100—120°)–*n*-butanol (6 : 4) saturated with water as solvent. Fractions were collected in the usual way and after evaporation of the solvent the syrups were dissolved in water and treated with charcoal. After filtration the solvent was removed, the products were taken up in acetone, and on removal of the acetone the following fractions were obtained.

Fraction	Substance	R_G	Wt. (g.)
A	2 : 3 : 4-Trimethyl mannose and 2 : 3-dimethyl methylmannoside	0·77	0·338
B	2 : 3-Dimethyl methylmannoside	—	0·046
C	Monomethyl methylmannoside	—	0·022
D	A dimethyl sugar	0·59	0·058
E	Mixture of D and F	0·54 & 0·59	0·204
F	2 : 3-Dimethyl mannose	0·54	1·151
G (water wash)	Monomethyl mannose	0·34	0·087

Fraction A (0·338 g.). This crystallised partly after being dried in a vacuum-desiccator, and had m. p. 68—71°, $[\alpha]_D^{15}$ −83·7° (*c*, 1·59 in water). 15·1 Mg. of the fraction on treatment with alkaline hypoiodite consumed 0·94 c.c. of 0·01N-iodine, indicating that only 6·9% of free reducing sugar, calculated as trimethyl mannose, was present. A portion of the fraction (0·259 g.) was rehydrolysed with sulphuric acid (2N; 10 c.c.; 3·5 hours) and chromatographic analysis of the product showed a considerable amount of 2 : 3-dimethyl mannose. The material was separated again on a cellulose column, but the new trimethyl fraction still contained a dimethyl mannoside as confirmed by a third hydrolysis (2N-H_2SO_4; 5·5 hours). Hypoiodite oxidation of the second hydrolysate indicated that 8·07% of free reducing sugar was present, equivalent to 1·09% of the original mixture of methylated mannoses (15·0 mg. consumed 1·09 c.c. of 0·01N-iodine). The difficulty of hydrolysis of 2 : 3-dimethyl methylmannoside is apparent from these results (compare Smith, *J. Amer. Chem. Soc.*, 1948, **70**, 3249, who found that methylmannoside required 25 hours at 95°).

A fourth hydrolysis was carried out with sulphuric acid (10 c.c.; 2N) for 7·5 hours, and the sugars were recovered in the usual way (0·128 g.). As the amount of trimethyl sugar was small, a separation of the tri- and di-methyl mannoses was effected on a wide strip of filter paper by heavy spotting of the solution along the starting line, two strips at the side being spotted separately as controls in a manner similar to that used for quantitative chromatography. After running for one night with *n*-butanol–ethanol–water solvent the side strips were developed with aniline oxalate solution, and the area of the centre strip containing the trimethyl sugar was cut out and extracted with boiling acetone from which the trimethyl mannose (8 mg.) was recovered by removal of the solvent *in vacuo*. Qualitative chromatography showed the presence of only one sugar in the syrup. This syrup was divided into two portions, one of which was subjected to demethylation with hydrobromic acid as described for Fraction D. The syrup thus obtained showed chromatographically the following sugars: 2 : 3-dimethyl mannose, R_G 0·54; monomethyl mannose, R_G 0·33; and free mannose, the presence of which was confirmed by comparison with controls. The other portion of the syrup was dissolved in water (2 c.c.) and oxidised with periodic acid (2 c.c.; 0·5M) for 40 hours, at the end of which the bulk of excess of periodate was removed as potassium periodate by addition of potassium chloride; the presence of formaldehyde was shown by the addition to the clear decanted solution of fresh solutions of phenylhydrazine hydrochloride and potassium ferricyanide, followed by two drops of concentrated hydrochloric acid: the characteristic port wine colour was then obtained. Of the trimethyl mannoses, only 2 : 3 : 4-trimethyl mannose would give formaldehyde on periodate oxidation.

Fraction B (0·046 g.). Rehydrolysis of this fraction showed that it consisted almost entirely of 2 : 3 dimethyl methylmannoside.

Fraction C (0·022 g.). Rehydrolysis of this fra ion showed that it consisted mainly of monomethyl methylmannoside.

Fraction D (0·058 g.). The syrup had OMe, 28·9%, and $[\alpha]_D^{15}$ +35° (*c*, 0·38 in water), suggestive of a dimethyl hexose. A portion of the syrup (5—10 mg.) was demethylated according to the method of Hough, Jones, and Wadman (*loc. cit.*) by treatment for 5 minutes in a sealed tube at 100° with hydrobromic acid (*d* 1·50; 1 c.c.), dilution with water (10 c.c.), neutralisation with silver carbonate, removal of silver ions with hydrogen sulphide, and recovery of the sugars as a syrup. Chromatographic examination showed the presence of glucose, a monomethyl sugar, R_G 0·27, and a little unchanged material. In a control experiment 3-methyl glucose

showed R_G 0·27. 2 : 3-Dimethyl mannose under the same conditions showed mannose, monomethyl mannose R_G 0·32, and the original sugar. These results indicate that this sugar is 2 : 3-dimethyl glucose and comparison with an authentic specimen showed that their R_G values were identical. The fraction was too small for further identification.

Fraction E. The syrup (0·204 g.) had OMe, 29·1% and, by use of a long filter strip (90 cm.), paper chromatography showed it to consist of two sugars, R_G values 0·54 and 0·59 respectively, identical with the sugar from Fraction D and 2 : 3-dimethyl mannose. A quantitative chromatogram was carried out in a similar way, the sugars being separated and their relative percentages determined by treatment with alkaline hypoiodite. Dimethyl glucose consumed 1·03 c.c., and dimethyl mannose 2·68 c.c., of 0·01N-iodine, indicating the presence of 27·7% of dimethyl glucose and 72·3% of dimethyl mannose.

Fraction F. The syrup (1·151 g.) had OMe, 27·4%, $[\alpha]_D^{15}$ −14·0 (*c*, 2·5 in water), and n_D^{15} 1·4830, and paper chromatography showed only one sugar to be present. On hypoiodite oxidation the syrup (2·2 mg.) consumed 2·00 c.c. of 0·01N-iodine, indicating a purity of 94·6%. Oxidation with bromine water converted the sugar into a lactone, $[\alpha]_D^{15}$ +67° falling to 58° after 7 days (equiv., 203). Oxidation of the syrup (31·4 mg.) with sodium metaperiodate (0·25M; 4 c.c.) for 18 hours resulted in the uptake of 1·75 mols. of $NaIO_4$ and the production of 0·85 mol. of formic acid per $C_8H_{16}O_6$ unit.

The syrup (0·178 g.) was treated with periodic acid (0·5M; 12 c.c.) for 24 hours, and the whole aërated for 18 hours to remove formaldehyde. To the solution were added barium chloride (0·6 g.) and excess of barium carbonate, and after filtration barium carbonate (0·5 g.) and bromine (1 c.c.) were added. Oxidation was allowed to continue for 36 hours, whereafter the bromine was removed by aëration. After neutralisation with silver carbonate, filtration, treatment with hydrogen sulphide, and filtration the solution was evaporated *in vacuo* to a solid. This was esterified by boiling methanolic hydrogen chloride (3%; 15 c.c.) for 16 hours, the solution neutralised with silver carbonate, and the solid obtained after filtration and evaporation was extracted with hot chloroform. The resulting extract on evaporation gave a thin syrup which crystallised on being dried overnight *in vacuo*. This was dimethyl *meso*dimethoxysuccinate, m. p. 65—66° not depressed on admixture with an authentic specimen (Found: C, 46·0; H, 7·1. Calc. for $C_8H_{14}O_6$: C, 45·5; H, 6·8%). *X*-Ray powder photographs of the two specimens were compared and the results confirmed the identity of the two samples.

Fraction G. The syrup (0·087 g.) had OMe, 12·0%. 3·4 Mg. consumed 2·47 c.c. of 0·01N-iodine during hypoiodite oxidation, indicating the presence of 70·7% of free reducing sugar as monomethyl hexose. Chromatographic investigation showed no sugars other than monomethyl mannose (R_G 0·34).

Effect of Lithium Aluminium Hydride on 2 : 3-Dimethyl Mannose.—In order to ascertain whether epimerisation of dimethyl mannose can take place during reduction with lithium aluminium hydride, a portion (0·226 g.) of Fraction F was converted into the methylmannoside by boiling methanolic hydrogen chloride (2%; 10 c.c.) during 7 hours. The methylmannoside was isolated as a syrup in the usual way ($[\alpha]_D^{15}$ +21°, n_D^{15} 1·4687). By following exactly the conditions of the original reduction, a syrup was obtained which showed, on chromatographic examination, none of the glucose derivative observed in the earlier experiments, indicating that under these conditions no epimerisation had occurred. The experiment did, however, suggest that the reduction procedure had involved some demethylation as a small amount of monomethyl mannose (R_G 0·34) was indicated on the chromatogram. This demethylation along with under-methylation probably accounts for much of the monomethyl mannose present in Fraction G.

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King's Buildings, University of Edinburgh.
Institute of Seaweed Research, Inveresk, Midlothian. [*Received, January 25th*, 1952.]

339. *Multiple Adaptations of* Bact. lactis aerogenes (Aerobacter aerogenes) *to Various Combinations of Substrate.*

By A. W. Scopes and Sir Cyril Hinshelwood.

Multiple adaptations of the cells of *Bact. lactis aerogenes* to various combinations of the following have been studied: glucose, glycerol, lactose, succinate, D-arabinose, proflavine, sulphanilamide.

Complete adaptation to more than one is possible, but more commonly there is a compromise with partial adaptation to the individual substances. Sometimes there is incompatibility, and in the case of proflavine and succinate there appears to be a relation between the two kinds of training. In general the adaptation is metastable in that it persists for long periods after removal of the cells from the substrate provoking it, but tends to be removed by appropriate disturbance of the cell economy.

The results are discussed in relation to the two theories of mutation and selection on the one hand and of growth-linked enzymic changes on the other. The second is to be preferred.

According to the chemical theory of the adaptive processes by which bacterial cells become resistant to drugs or utilise new substrates with increased efficiency, the adaptation is essentially reversible, but may show in appropriate circumstances a very considerable degree of metastability (*J.*, 1952, 745).

On transfer to a new medium, increase in growth rate and decrease in lag (the induction period preceding cell multiplication) may occur on continued subculture, and on return to the original medium this so-called training may or may not be lost—as shown by further tests in the second medium. A variety of cases are considered in the paper referred to, and the object of the present study is to illustrate the kinds of behaviour found by experiment on multiple adaptations.

The methods of experiment were as described previously. By training is meant serial subculture of cells in a given medium, the extent of the process being measured by the mean generation time (time taken for number of cells to double in logarithmic growth), and by the lag (intercept of logarithmic growth curve on time axis).

Previous observations in this laboratory made in this way have shown that *Bact. lactis aerogenes* may be trained to show optimum growth rate in maltose, sucrose, and lactose (parallel tests in the three sugars), that this state is compatible with optimum behaviour in glucose (Postgate and Hinshelwood, *Trans. Faraday Soc.*, 1946, **42**, 45), that optimum growth rate in glycerol may be retained during many intervening passages through glucose (Cooke and Hinshelwood, *ibid.*, 1947, **43**, 733), and that, in general, the simultaneous holding of different kinds of training is possible. The theory suggests that, in general, the relations should be rather more complex, and that there should, in some cases at least, be a certain measure of competition between the various forms of adaptation.

The organism used for the present experiments was a strain of *Bact. lactis aerogenes* which has been maintained for some years in the laboratory. The growth media used consisted of phosphate buffer, ammonium sulphate, magnesium sulphate, and the carbon source to which the cells were to be adapted. Where necessary, appropriate amounts of antibacterial drugs were added. When adaptations to more than two substrates were investigated, the bacteria were subcultured successively in the relevant media and then tested simultaneously in them all. Under the standard condition employed a subculture represents about 8—10 successive cell divisions.

In the tables of results the following abbreviations are employed:

G	glucose	Su	succinate
Gy	glycerol	A	D-arabinose
L	lactose	B	broth

Pf indicates a glucose medium containing 2 : 8-diaminoacridine (proflavine) and Sa a similar medium containing sulphanilamide. The history of a strain is indicated as in the following example : A54.Su6.Gy4 means that there had been 54 subcultures in D-arabinose, followed by 6 in succinate and then by 4 in glycerol.

The concentrations of the carbon sources (which are of little influence on lag or growth rate) were from 5 to 25 g./l. as was convenient.

Arabinose–Lactose.—Three strains were investigated, namely A5, A23, and A46, and the behaviour on training to lactose was found to be a function of the number of preliminary subcultures in arabinose. Typical results are shown in Table 1. The symbol ∞ indicates the limiting condition reached after prolonged training.

TABLE 1.

	Strain	M.g.t. (min.)	Lag (min.)
(*a*)	A1	>200	>1500
	A_∞	58	0
	L1	65	100—200
	L_∞	35	0

	Strain	M.g.t. (min.) in A	M.g.t. (min.) in L	Lag (min.) in A	Lag (min.) in L
(*b*)	A5.L8	—	46	100	0
	A5.L35	156	35	580	0
	A5.L45	129	35	850	0
(*c*)	A23.L1	51	48	0	30
	A23.L36	198	34	460	0
	A23.L71	208	38	770	0
(*d*)	A46.L1	63	56	0	0
	A46.L11	75	40	0	0
	A46.L53	68	35	500	0
	A46.L80	77	35	350	0

Comparison of (*b*), (*c*), and (*d*) shows that the arabinose adaptation is more tenaciously held on passage through lactose the longer it has originally been impressed, that a high degree of training to both sugars can be held simultaneously (A46.L11), but that there is competition even in (*d*), where eventually the lag in arabinose shows quite a marked increase. On the other hand, comparison with (*a*) shows that reversion to the untrained state does not come about even in 80 subcultures.

The results of training in the reverse order are shown in Table 2.

TABLE 2.

Strain	M.g.t. (min.) in A	M.g.t. (min.) in L	Lag (min.) in A	Lag (min.) in L
L40	—	35	—	0
L40.A1	250	42	450	0
L40.A3	75	47	—	—
L40.A12	74	45	0	80
L40.A59	49	47	0	120

Comparison with Table 1(*a*) shows that, although even after prolonged passage through the second medium the adaptation to the first is considerably above that of an untrained strain, nevertheless a certain degree of competition is evident. When fully adapted to arabinose the strain has lost some of its adaptation to lactose.

Succinate–Glycerol.—The compatibility of the two kinds of adaptation is here partial. The actual behaviour in the succinate medium shows quite considerable fluctuations, the growth rate being a function of the immediate past history (probably of the precise age of the parent culture). Typical results are shown in Table 3.

The succinate-trained strain does not take the glycerol training completely : nor does it retain quite the full amount of its adaptation to the succinate on passage through glycerol. These facts are revealed by the values of the m.g.t., the lags showing only unimportant fluctuations. (It should be noted that lag is a function of the age of the inoculum, and

that although this is controlled minor fluctuations of an hour or so are of little significance. Real loss of adaptation would be reflected in a lag of at least four hours.)

TABLE 3.

	Strain	M.g.t. (min.)	Lag (min.)
(*a*)	Su1	120—230	500
	Su_{∞}	35	0
	Gy1	Variable	250
	Gy_{∞}	35	0

		M.g.t. (min.) in		Lag (min.) in	
	Strain	Su	Gy	Su	Gy
(*b*)	Su6.Gy1	82	39	0	240
	Su6.Gy10	64	49	140	0
	Su6.Gy43	61	41	0	50
	Su6.Gy57	56	45	0	110

Succinate–Arabinose.—A strain which had been trained in succinate for a considerable, but not recorded, number of subcultures was subcultured into arabinose and eventually became moderately well adapted to both substrates. There were some signs of a competition between the two types of adaptation (Table 4). The variations in lag, although appreciable and indicative of impaired adaptation, have to be compared with the value of *ca.* 3000 min. for the untrained strain.

TABLE 4.

	Strain	M.g.t. (min.)	Lag (min.)
(*a*)	Su1	120—230	500
	Su_{∞}	35	0
	A1	300	*ca.* 3000
	A_{∞}	58	0

		M.g.t. (min.) in		Lag (min.) in	
	Strain	Su	A	Su	A
(*b*)	Su *x*.A1	60	300	—	530
	Su *x*.A7	44	145	0	530
	Su *x*.A25	83	68	0	60
	Su *x*.A34	66	57	0	400

Arabinose–Lactose–Succinate.—A strain A46.L84 which had been stored in broth for some time without any noticeable change in the state of adaptation was given further passages through arabinose and lactose, and at the end of this process showed a high degree of adaptation to both, as shown in Table 5(*a*). It was then subcultured in succinate, during which process a very considerable impairment of the adaptation to the first two sugars was observed (Table 5*b*).

TABLE 5.

		M.g.t. (min.)			Lag (min.)		
	Strain	A	L	Su	A	L	Su
(*a*)	A1	200	—	—	1500	—	—
	L1	—	65	—		100—200	
	Su1	—	—	120—230	—	—	500
	A_{∞}	58	—	—	0	—	—
	L_{∞}	—	35	—	—	0	—
	Su_{∞}	—	—	35	—	—	0
	A46.L84.B1.A10.L9	66	36	—	0	25	—
(*b*)	A46.L84.B1.A10.L6.Su6	350	200	37	500	250	60
	A46.L84.B1.A10.L6.Su17	350	—	—	700	700	0

The disorganisation of the arabinose–lactose training by the subsequent training to succinate is the most marked competitive effect so far encountered in this series of tests.

Arabinose–Lactose–Succinate–Glycerol.—Several arabinose–lactose trained strains were subcultured successively in succinate and in glycerol. The adaptation to arabinose and

lactose was impaired by this process to varying extents: the glycerol adaptation was imperfect and the succinate adaptation, although not complete, was nearly so. The results are summarised in Table 6.

TABLE 6.

	M.g.t. (min.)				Lag (min.)			
Strain	A	L	Su	Gy	A	L	Su	Gy
A5.L66.Su6.Gy6	55	34	50	75	1400	130	160	270
A23.L42.Su6.Gy6	128	34	54	41	1400	120	130	90
A46.L27.Su6.Gy6	119	46	48	49	800	80	140	25

Proflavine–Succinate.—The strain was trained to grow without lag at a concentration of 100 mg. of proflavine per l. (glucose medium) and was then passed through succinate. From the beginning it showed a considerable degree of adaptation, the m.g.t. being 36 min. and the lag 70 min. only. After 22 passages through succinate the m.g.t. in the medium was 40 min., and the lag in the proflavine–glucose medium was still zero, although the m.g.t. had risen from 45 to 66 min. These results indicate not only a compatibility of the two types of training, but even a certain degree of inter-relationship.

Proflavine–Glycerol.—The proflavine-trained strain was transferred to a glycerol medium, in which adaptation proved to be definitely more difficult than that of the normal strain. After 20 passages the m.g.t. was still 50 min., compared with the value 35 min. reached in normal training by transfer from glucose. These subcultures in glycerol increased the m.g.t. in presence of proflavine from 45 to 68 min. The lag, however, which for the untrained strain would have been over 7 days at 100 mg. of proflavine per l. was still no more than 110 min.

Proflavine–Arabinose.—The trained strain showed considerable resistance to adaptation to D-arabinose, the m.g.t. after 12 subcultures still being as high as 140 min., compared with 76 in a control experiment with an untrained strain also passed 12 times through the arabinose.

Proflavine–Lactose.—After about 8 subcultures the proflavine-trained strain became more or less fully adapted to lactose. After 12 passages in the lactose it had increased its m.g.t. in the drug medium from 45 to 97 min. The lag, however, remained nearly zero.

Sulphanilamide–Glycerol.—Complete adaptation to both drug and carbon source was reached by training first to 1000 mg. of sulphanilamide per l., and then subjecting the strain to 20 passages in glycerol. The final m.g.t. in glycerol was 35 min., and that in the glucose medium with drug 36 min. The lags both approximated to zero. The rate of adaptation of the drug-trained strain to the glycerol was rather slower than normal.

Sulphanilamide–Succinate.—The results were generally similar to those found with glycerol.

Sulphanilamide–Arabinose.—Complete training to the arabinose was attained after about 20 subcultures (m.g.t. 58 min., lag zero). The rate of training appeared to be lower than normal.

Sulphanilamide–Lactose.—The strain trained to 1000 mg. of sulphanilamide per l. showed considerable resistance to training to lactose. There was a long lag on the first transfer, and this persisted through several subcultures. Eventually after 50 subcultures the lag was zero and the m.g.t. 35 min.

Proflavine–Sulphanilamide–Succinate.—The strain trained to 100 mg. of proflavine per l. was subcultured successively in sulphanilamide media containing respectively 250, 500, and 1000 mg./l. and then passed further through the last of these. It was then trained to succinate in parallel with a culture transferred directly from the usual glucose medium. These two strains showed parallel behaviour except that the drug-trained bacteria had already acquired some degree of adaptation to the succinate.

Proflavine–Sulphanilamide to Arabinose, Glycerol, or Lactose.—In all cases the strain trained to the two drugs offered some resistance to further training, especially with lactose, but the final state was not investigated.

Proflavine–Arabinose–Succinate.—A strain was fully trained to 100 mg. of proflavine

per l. and then subcultured 14 times in D-arabinose and 14 times in succinate. It then proved to be fully trained to none of these, but to show a better performance in all media than the untrained strain would have shown, that is, a compromise seemed to have been reached. The lag in succinate was zero, but the m.g.t. was ten minutes higher than that of the fully trained strain. In arabinose the m.g.t. was 205 min., and the lag 750 min. (compared with zero for the fully trained strain and over 1500 min. for the normal strain). In proflavine at 100 mg./l. the m.g.t. was 64 and the lag 1000 min. (optimum value zero, original value >7 days).

Proflavine–Arabinose–Lactose.—The proflavine-trained strain (as above) was given 14 passages in arabinose and 14 in lactose. As a result the strain was nearly fully adapted to lactose (lag 70 min. and m.g.t. 42 min. compared with 35 for complete adaptation). The lag in arabinose was 1000 min. and the m.g.t. 66 min. (optimum 58 min. and original >200 min.). The lag in proflavine had risen to more than 24 hours.

Once again, competition and compromise are apparent.

Proflavine–Sulphanilamide–Succinate–Glycerol.—The proflavine-trained strain was passed through sulphanilamide four times (the concentration being increased to 1000 mg./l.) and then given 6 passages in succinate and 6 in glycerol. The lag in proflavine remained quite short (300 min.) but the m.g.t. increased to 77 min. The succinate training was complete, but in glycerol the m.g.t. was 163 min. compared with the optimum of 35 min. Tested in sulphanilamide at 500 mg./l. the strain showed zero lag, but an m.g.t. of 78 min.

Proflavine–Sulphanilamide–Succinate–Glycerol–Lactose.—The strain finally tested was Pf*x*.Sa4.Su6.Gy5.L8, *x* being a very large number. It showed a lag of 1150 min. in proflavine at 100 mg./l. (cf. >7 days and zero for the extremes): in sulphanilamide at 500 mg./l. the lag was 200 min. The results are summarised in Table 7.

TABLE 7.

	M.g.t. (min.) in				
	Pf	Sa	Su	Gy	L
Multiply-trained strain	85	45	58	42	200
Optimum	45	33	35	35	33
	Lag (min.) in				
	Pf	Sa	Su	Gy	L
Multiply-trained strain	1150	200	0	250	600
Optimum	0	0	0	0	0
Initial value	>7 days	—	500	250	200

The lactose-adaptation has been very adversely affected. In the other cases there is some sort of a compromise.

Transfers between Glucose Media with and without Proflavine.—After adaptation to proflavine the growth rate in glucose of the normal strain is found to be lowered. Judging from the changes brought about by acriflavine in yeast cells one may infer that some of the oxidative mechanisms of the cell have been damaged (Slonimski and Ephrussi, *Ann. Inst. Pasteur*, 1949, **77**, 47). Serial subculture in the original drug-free glucose medium restores the normal growth rate, and it now becomes a matter of interest to know how the proflavine adaptation fares during this " re-training " to normal behaviour in glucose.

The normal strain of *Bact. lactis aerogenes* was transferred from the usual glucose medium to one containing 20 mg. proflavine per l. and then successively to media containing increasing amounts up to 90 mg./l. At intervals during the training process the growth characteristics were measured, both in the medium containing the highest concentration of proflavine to which the cells had so far been exposed, and in the drug-free medium. Various trained strains were then tested at intervals during serial passage through the glucose medium, and when they were found to have returned almost to normal were retested in presence of proflavine for retention or loss of adaptation. Sugar tests were also made at intervals (according to the procedure laid down in Reports on Public Health and Medical Subjects, No. 71, The Bacteriological Examination of Water Supplies, H.M.S.O., 1939).

The results of these experiments are summarised in Table 8. For small degrees of proflavine-adaptation the growth rate in the glucose medium is not noticeably impaired. But as training is carried further the trained strain shows signs of damage, the m.g.t. in the drug-free medium rising to over 40 min. Serial passages bring this back to normal. At the end of the re-training process the proflavine-adaptation itself shows signs of appreciable regression, but is still much greater than it was for the original untrained strain, lags of 3—6 hours having developed in place of zero for the fully trained cells but in place of more than 24 hours for the original.

TABLE 8.

History of training: subcultures in Pf medium at mg./l.				M.g.t. in Pf at max. conc. in training (min.)	M.g.t. in glucose medium after number of "re-training" subcultures shown in parentheses (min.)	Test of "re-trained" strain in Pf: m.g.t. (min.)	Test of "re-trained" strain in Pf: lag (hr.)
20	40	60	70	—	—	—	—
1				—	(2)29, (4)32	—	—
3				—	(2)29	—	—
3	2			—	(3)32	—	—
3	3			55	(2)46, (3)32, (4)42, (10)35	—	—
3	3	3		49	(3)45, (10)40, (12)40, (17)32	—	10
3	3	6		—	(4)41, (9)41, (14)39, (16)31	50	5·5
3	3	6	1	—	(3)48, (8)47, (13)52, (15)37, (17)34	50	6
3	3	6	4	—	(4)47, (6)49, (9)42, (11)36, (13)38	51	5

Notes: The subcultures recorded under history of training are additive. The lags in the last column would all have been well over 24 hours for untrained strains.

In these experiments the training was carried up to 90 mg./l. The m.g.t. in presence of proflavine was then 56 min. and the lag zero. The initial value of the m.g.t. found on testing in the drug-free glucose medium was, in different tests, 36, 44, and 37 min. and in 8 or 9 subcultures in glucose it had not returned fully to normal.

The strain after 8 passages at 70 mg./l. and one at 80 mg./l. showed an m.g.t. on return to the drug-free medium, which fell from 47 to 33 at the 6th passage and rose to 36 min. at the 8th. The lag in the proflavine medium was then 3½ hr.

The sugar tests of the proflavine-trained strain were in some respects abnormal, notably in failure to give acid and gas with sucrose. The Voges–Proskauer test was also negative. Subsequent passage through drug-free glucose medium restored these tests to normality.

DISCUSSION

One general conclusion that can be reached is that with this organism nearly complete training to two or more substrates can occur, but that more usually there is a compromise. The first type of case seems to be characteristic of substances which are metabolised by similar reaction routes, for example, glucose and glycerol, arabinose and lactose. The second type probably indicates a competition between metabolic routes: it is exemplified by the system succinate–lactose, where the incompatibility is rather marked.

Evidence exists for the presence of alternative routes of this kind. In the re-training in glucose of the proflavine-damaged strains composite growth curves showing two phases, one of longer, the other of shorter m.g.t., were sometimes observed. This happens when growth by one route with a shorter lag is superseded by more rapid growth associated with a longer lag (cf. Dean and Hinshelwood, *J.*, 1951, 1157).

Training to drugs is compatible with adaptation to carbon substrates, but various specific influences are in evidence. The example of proflavine is interesting. As has been pointed out, this substance causes damage to the oxidative mechanisms of the cell, according to Slonimiski and Ephrussi (*loc. cit.*) to the cytochrome system. According to Keilin and Hartree (*Proc. Roy. Soc.*, 1940, *B*, **129**, 227) the succinic dehydrogenase system is closely related to cytochrome. Prolonged training to proflavine may, therefore, lead to an increase in the amount of this system to compensate for its decreased activity. On transfer of the trained cells to succinate, therefore, they may well prove to be much more fully adapted than normal cells, as indeed is found.

Another important characteristic of the general picture presented by these results is that the state of the trained bacterial cell is more often metastable than stable, and, although

the adaptation may show a high degree of persistence, it does suffer slow changes on very prolonged subculture. The stability is in a large measure a function of the adaptive history, as illustrated by the results for arabinose and lactose.

About the general interpretation of adaptive phenomena, there are, of course, two schools of thought. According to one, training depends upon chance mutation of genes followed by the selection of those mutants which are favoured by the particular environment. According to the other, modification of the enzymic make-up of the cell occurs in response to changed reaction rates, in the manner outlined in a previous paper (*J.*, 1952, 745).

In its application to the present results the mutation-selection theory demands several special assumptions which detract from its probability. The process of training is often slow, gradual, and continuous. There is no rapid emergence of a fully adapted mutant strain as there would be if the change were controlled by a single major mutation. It is necessary to postulate a system of polygenes, so that at any stage the differences between individuals are small. Loss of training has to be attributed to reverse mutations, and where a compromise between two types of adaptation is reached this has to be explained by a selection of polygenes after the appropriate and rather elaborate series of mutations and reverse mutations. To account for the dependence of persistence on previous history it may also be necessary to postulate special genes controlling, not only the character, but also the stability of the training.

Such assumptions are not impossible ones, but they are not based upon any very probable physico-chemical grounds. On the other hand, the hypothesis of changed enzyme constitution, although not without its own complications, is more satisfactory from a chemical point of view. It is, indeed, itself a selection theory in one sense, since the changes in enzyme proportions which are brought about by altered reaction rates themselves constitute an internal selection of one type of matter within all the cells, compared with the selection of a few special cells. Both kinds of effect may in fact occur, but the reference of the adaptation to the bulk of the population is to be preferred, for the examples considered, in view of the fact that in several similar cases there is direct evidence for the response of the majority of the cells (Jackson and Hinshelwood, *Proc. Roy. Soc.*, **1949**, *B*, **136**, 562; **137**, 88; Baskett and Hinshelwood, *ibid.*, **1951**, *B*, **139**, 58; Kilkenny and Hinshelwood, *ibid.*, p. 73; Baskett, *ibid.*, in the press; Dean and Hinshelwood, *J.*, **1951**, 1157). According to the theoretical findings of the earlier paper (*J.*, **1952**, **745**) there should, on the whole, be some degree of antagonism between different adaptations, unless the enzymes concerned are closely related, or unless an enzyme capable of handling both substrates is present. With glucose–arabinose or glucose–glycerol this may occur. With adaptation to proflavine and succinate there is also the possibility that a common enzyme system expands during the training. But more often apparent compatibility of training is to be explained in terms of metastability and slowness of reversion, and this idea seems in general to be borne out by the experiments. One of the cases dealt with theoretically envisaged an increase in lag in an original substrate caused by intervening passages in a second substrate: there are several indications of such an effect among the experimental results described.

PHYSICAL CHEMISTRY LABORATORY,
UNIVERSITY OF OXFORD.

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340. *A Polarographic Investigation of the Redox Behaviour of Certain Hydroxy- and Sulphonic Acid Derivatives of Anthraquinone.*

By R. Gill and H. I. Stonehill.

The redox potential (E) and semiquinone formation constant (K) have been determined polarographically at 25° for aqueous solutions of the 1- and 2-sulphonic acid, and the 1- and 2-hydroxy- and 1 : 2-, 1 : 4-, 1 : 8-, and 2 : 6-dihydroxy-derivatives of anthraquinone, over the pH range 7—13 approx., at constant ionic strength. The reversibility of the polarographic oxidation–reduction is demonstrated by the agreement with earlier potentiometric results for some of the compounds, as well as by the independence of the results of the state of reduction of the solutions polarographed, except for the 2-hydroxy- and 2 : 6-dihydroxy-compounds, which in the reduced state tautomerise (see following paper).

Semiquinone formation is favoured by the increased ionisation at high pH, but is not completely absent even at the lowest pH used. The influence of the substituent groups on E and K for the fully ionised compounds is explained in terms of inductive, resonance, and *ortho*-effects. Addition of ethanol renders E more negative, increases K, and decreases diffusion current constant, and increase of ionic strength at constant pH in aqueous solutions renders E more negative and decreases K, although superimposed repression of ionisation complicates both the latter sets of observations. There is no evidence for association or polymerisation of any of the compounds in any state of oxidation or ionisation.

As a preliminary to the polarographic examination of some anthraquinonoid dyes, we have thought it desirable to investigate polarographically the redox behaviour of a series of substituted anthraquinones. The only published detailed investigation in this field by the same technique is by Furman and Stone (*J. Amer. Chem. Soc.*, 1948, **70**, 3055), who briefly summarise earlier work. The present investigation was completed before that paper appeared (cf. Gill, Thesis, London, 1948), and the two investigations cover some common ground, although the results are not always in agreement.

Many quinonoid systems have been shown to undergo reversible polarographic reduction, giving half-wave potentials E_m equal to potentiometrically determined virtual standard redox potentials $E^{\circ\prime}$ for a given pH, and in some cases semiquinone formation constants K (where applicable) in fair accord with potentiometric values. Such agreement has been found for *p*-benzoquinone (Müller and Baumberger, *Trans. Electrochem. Soc.*, 1937, **71**, 169, 181; Müller, *J. Amer. Chem. Soc.*, 1940, **62**, 2434; Kolthoff and Orlemann, *ibid.*, 1941, **63**, 664), *o*-xyloquinone, 4 : 7-indanequinone and 1 : 2 : 3 : 4-tetrahydro-5 : 8-naphthaquinone (Arnold and Zaugg, *ibid.*, 1941, **63**, 1317), *p*-benzoquinone, toluquinone, *p*-xyloquinone, duroquinone, and 2 : 3-dimethyl-1 : 4-naphthaquinone (Smith, Kolthoff, Wawzonek, and Ruoff, *ibid.*, 1941, **63**, 1018), α-hydroxyphenazine (Müller, *Cold Spring Harbor Symp. Quant. Biol.*, 1939, **7**, 59), and methylene-blue (Brdička, *Z. Elektrochem.*, 1942, **48**, 278). Even when the polarographic reduction (or oxidation of the corresponding reduced species) is irreversible, apparent K values, calculated on the assumption of reversibility, may sometimes be related significantly to other properties of the system which involve semiquinone formation, as, *e.g.*, for acridine and its amino-derivatives (Kaye and Stonehill, *J.*, 1951, 27, 2638), for crystal-violet, brilliant-green, and auramine, and for riboflavin, cozymase, Nile-blue, Capri-blue, and cresyl-blue (*J.*, in preparation).

We shall therefore regard polarographic current–voltage oxidation (reduction) waves as theoretically equivalent to potentiometric oxidative (reductive) titration curves, the ratio of the polarographic current at any point (reckoned from the bottom of the wave as zero) to the diffusion current or total wave-height being treated as the fractional extent of oxidation, α (reduction, $1 - \alpha$), and E_m as if it were $E^{\circ\prime}$ (cf. Kolthoff and Lingane, "Polarography," Intersci. Publ., New York, 1941, p. 185). This equivalence requires, apart from reversibility, the reasonable assumptions that the diffusion coefficients of the

reduced, oxidised, and semiquinone forms of the electroactive material are all equal, and that the concentration gradient between the dropping-mercury electrode (d.m.e.) surface and the bulk of the solution is linear.

Experimental

Materials.—Anthraquinone 1- and 2-sulphonic acids (commercial) were recrystallised four times from water. Commercial anthraquinone 1 : 2-dihydroxy-3-sulphonic acid (alizarin-red S) was recrystallised twice from water; some difficulty was encountered, owing to its high solubility. Commerical alizarin paste was dried and extracted (Soxhlet) with glacial acetic acid, and the evaporated extract recrystallised three times from this solvent, and then twice from 95% ethanol. 2-Hydroxy- and 2 : 6-dihydroxy-anthraquinone (commercial) and technical "pure" 1-hydroxy- and 1 : 4- and 1 : 8-dihydroxy-anthraquinone were recrystallised four times from 95% ethanol. In each case the progress of purification was checked by comparing polarographic wave-height at a given concentration before and after the final recrystallisation. Ethanol was the middle cut from the fractional distillation of "absolute" alcohol. It was checked for the absence of any polarographically active impurities by determining the residual current of 0·1N-sodium hydroxide in water containing 50% by volume of the ethanol.

Sodium hydroxide, potassium chloride, and all buffer constituents were of "AnalaR" grade. Commercial sodium dithionite (hydrosulphite, Brotherton's Ltd.), described as 98—99% pure, was used as received. Mercury was redistilled, treated with mercurous nitrate solution, washed with distilled water, then acetone, and finally dried.

Apparatus.—A manual polarographic circuit was used. The potential was applied to the cell by a potential divider giving steps of 1/1000 of the full range, which was adjustable from ±4 v to ±0·2 v by additional series resistances. The polarographic current was measured by determining the voltage drop across a standard resistance in series with the cell, a Tinsley potentiometer being used and, as null instrument, a sensitive moving-coil galvanometer with lamp and scale; the galvanometer was shunted to damp excessive oscillations caused by variation of current during drop-life. Current accuracy was 0·005 μamp. up to 2 μamp., 0·01 μamp. between 4 and 6 μamp., and 0·03 μamp. between 8 and 10 μamp., the accuracy decreasing with increasing current because of the need for heavier damping by shunting. The polarographic cell was essentially similar to that described by Kaye and Stonehill (*J.*, 1951, 27), but in order to add dithionite to the cell contents when necessary, the cell was provided with a 1-ml. microburette, fitted by means of a ground-glass joint into a tube passing through the stopper at the top of the cell. The immersion-type saturated calomel electrode, against which the potential of the dropping-mercury electrode was measured to within 0·1 mv with the same potentiometric equipment as used for current measurement, employed electrolytic calomel (Lipscomb and Hulett, *J. Amer. Chem. Soc.*, 1916, **38**, 21). The hand-drawn Pyrex capillary had the following characteristics: drop time $t = 4{\cdot}68$ seconds with no applied potential; mercury flow rate $m = 0{\cdot}924$ mg./sec. in aqueous phosphate buffer at pH 11·27, ionic strength 0·1, at 25°. The capillary was connected to the mercury reservoir by a short glass tube in order to avoid any contact of rubber with the mercury. The small pressure due to the short head of mercury was supplemented by connecting the stoppered reservoir with a length of rubber pressure tubing to a 2-litre air-pressure reservoir bottle fitted with a mercury manometer and pressure-release cock, and charged with air *via* a cycle-tyre valve by using a cycle pump. The cell was kept at 25° ± 0·01°, unless otherwise stated, by means of a water thermostat bath.

Procedure.—Known weights of the anthraquinones were dissolved in suitable buffers of known pH and ionic strength as supporting electrolytes, and the solutions added to the cell and deoxygenated by bubbling purified cylinder nitrogen through them for 30 minutes. The nitrogen was purified by passage through two 1-metre columns packed with copper gauze kept moistened with saturated ammonium carbonate–concentrated ammonia mixture by means of lift-pump circulators (Kraus and Parker, *J. Amer. Chem. Soc.*, 1922, **44**, 2429) to remove oxygen, then through wash-bottles containing successively dilute sulphuric acid and concentrated sodium hydroxide solution to remove ammonia, acid spray, and carbon dioxide. The efficiency of deoxygenation of the nitrogen was demonstrated by the polarographic indication that the percentage reduction in a 4×10^{-4}M-solution of anthraquinone-2-sulphonic acid in 0·1N-sodium hydroxide, half-reduced with sodium dithionite, was unchanged after passing the gas stream through it for 30 minutes. In cases where the solubility of the anthraquinone compound was too low in the buffer supporting electrolyte, a solution suitable for

polarography was prepared by suspending the solid compound in supporting electrolyte in the cell, deoxygenating it for 20 minutes, adding a known quantity of standard dithionite solution from the microburette, sufficient to cause partial or complete reduction, and bubbling nitrogen for at least a further 10 minutes to ensure complete reaction. Polarograms were generally corrected for residual currents, which were determined on the pure supporting electrolytes.

Results.—(1) *Sodium dithionite.* Although it would have been preferable to reduce the anthraquinones to their leuco-compounds catalytically with hydrogen and platinum or palladium, rather than by adding dithionite and thus affecting the ionic strength and composition of the solution, the highly negative reduction potentials of the anthraquinones render this impracticable (Burstein and Davidson, *Trans. Electrochem. Soc.*, 1941, **80**, 175). It was obviously desirable to examine the polarographic behaviour of the sodium dithionite used. Two independent samples gave identical polarograms, typified by Fig. 1*a*. The half-wave potentials of the various waves were scarcely affected by varying the pH over the range 8—13, but the relative wave-heights were somewhat dependent on pH. This suggests that the small waves may be due to substances (or to oxidation and reduction respectively of a single substance) in equilibrium with

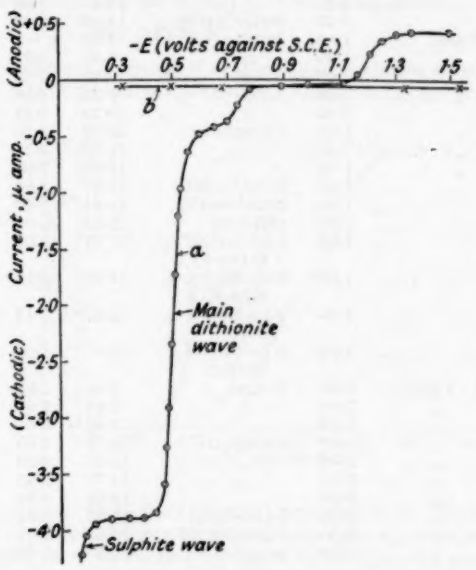


FIG. 1. *Polarograms for sodium dithionite (0·170 g./l.) in 0·1N-NaOH, 25° (uncorrected for residual current).*

a, In oxygen free solution.
b, After atmospheric oxidation.

dithionite. In support of this view, the solution of dithionite, after oxidation by contact with air overnight, gave a polarogram (Fig. 1*b*) in which all waves had disappeared, including the cathodic wave at about −1·205 v, which would probably have been unaffected by oxidation had it been due to an impurity not in equilibrium with dithionite. No further investigation was made, however, as the suitability of the sodium dithionite for the present purpose is adequately demonstrated by Fig. 1*b*, which shows that, provided no excess unused dithionite be present, no interfering polarographic waves due to oxidation products of the dithionite will appear over the potential range employed in polarographing the anthraquinones. Brearly and Starkie (*J. Soc. Dyers Col.*, 1948, **64**, 278) obtained for zinc dithionite in ammonium phosphate a single anodic wave at −0·4 v against the saturated calomel electrode, obviously distinct from waves for sulphite, thiosulphate, and sulphide in the same medium, which start at −0·1, −0·2, and −0·8 v, respectively.

(2) *Anthraquinone-2-sulphonic acid.* This substance was chosen for preliminary work in establishing the applicability of polarography to semiquinone-constant investigation, because its reversible redox characteristics have been well investigated by potentiometric titration (Conant, Kahn, Fieser, and Kurtz, *J. Amer. Chem. Soc.*, 1922, **44**, 1382; Geake and Lemon, *Shirley Inst. Mem.*, 1937—38, **16**, 111, 125; *Trans. Faraday Soc.*, 1938, **34**, 1409; Burstein and Davidson, *loc. cit.*). Typical polarograms are shown in Figs. 2*a*, *b*, and in Table 1 are listed for

TABLE 1. *Results for aqueous solutions.*

Substituents	*c*	Supporting electrolyte *	pH	*d*	$-E_m$ (v)	$-E_1$ (v)	$-E_2$ (v)	$\sqrt{R}$	*I*
1-SO_3H ...	0·4	0·1N-NaOH	12·87	3·00	0·6774	—	—	0·47	0·1
,, ...	1·0	,,	12·87	2·97	0·6748	—	—	0·39	0·1
2-SO_3H ...	2·0	Borate	6·14	—	0·413	—	—	—	0·1
,, ...	2·0	,,	6·97	—	0·460	—	—	—	0·1
,, ...	2·0	,,	7·82	—	0·506	—	—	—	0·1
,, ...	0·314	,,	7·82	3·02	0·5064	—	—	0·24	0·1
,, ...	2·0	,,	8·69	—	0·553	0·584	0·522	0·30	0·1
,, ...	2·0	,,	9·48	—	0·576	0·602	0·550	0·36	0·1
,, ...	2·0	,,	10·23	—	0·595	0·602	0·588	0·76	0·1
,, ...	2·0	Phosphate	11·17	—	0·614	0·602	0·626	1·71	0·1
,, ...	2·0	,,	12·00	—	0·617	0·600	0·634	1·94	0·1
,, ...	1·705	,,	12·58	3·00	0·6183	0·6013	0·6353	1·94	0·1
,, ...	2·0	0·1N-NaOH	12·87	—	0·618	0·600	0·636	2·02	0·1
1-OH	1·00	Phosphate	12·00	—	0·6831	—	—	0·24	0·1
,, ...	0·402	0·1N-NaOH	12·87	2·91	0·7118	—	—	0·22	0·1
,, ...	2·29	,,	12·87	2·86	0·7098	—	—	0·35	0·1
,, ...	1·35	0·25N-NaOH	13·25	2·93	0·7178	—	—	0·14	0·25
2-OH	1·00	Borate	8·15	—	0·630	—	—	—	0·1
,, ...	1·00	,,	8·85	3·04	0·6882	0·7167	0·6597	0·33	0·1
,, ...	1·00	,,	9·59	3·09	0·7314	0·7591	0·7037	0·34	0·1
,, ...	1·00	,,	9·95	3·07	0·7462	0·7724	0·7200	0·36	0·1
,, ...	1·00	,,	10·22	3·13	0·7615	0·7820	0·7410	0·45	0·1
,, ...	1·00	Phosphate	10·79	3·16	0·7732	0·7863	0·7601	0·60	0·1
,, ...	1·00	,,	11·27	3·12	0·7910	0·7949	0·7871	0·86	0·1
,, ...	1·00	,,	12·00	3·03	0·8112	0·7966	0·8258	1·77	0·1
,, ...	1·00	0·1N-NaOH	12·87	3·08	0·8258	0·7948	0·8570	3·32	0·1
,, ...	1·00	0·25N-NaOH	13·25	3·02	0·824	0·792	0·856	3·49	0·25
,, ...	1·00	N-NaOH	13·82	3·00	0·827	0·794	0·860	3·56	1·0
,, ...	1·00	0·1N-NaOH + 0·15N-KCl	12·87	3·08	0·8163	—	—	2·96	0·25
,, ...	1·00	0·1N-NaOH + 0·5N-KCl	12·87	3·12	0·8104	—	—	2·54	0·6
,, ...	1·00	0·1N-NaOH + N-KCl	12·87	3·13	0·8072	—	—	2·04	1·1
,, ...	1·00	0·1N-NaOH + 2N-KCl	12·87	3·04	0·8008	—	—	1·59	2·1
1 : 2-$(OH)_2$	2·00	Borate	7·82	2·85	0·5528	—	—	—	0·1
,,	2·00	,,	8·69	2·88	0·6080	—	—	—	0·1
,,	2·00	,,	9·67	2·90	0·6730	0·6884	0·6576	0·55	0·1
,,	2·00	Phosphate	10·79	2·89	0·7680	0·7775	0·7585	0·69	0·1
,,	2·00	,,	11·27	2·89	0·8058	0·8061	0·8055	0·99	0·1
,,	2·00	,,	11·77	2·92	0·8352	0·8222	0·8482	1·66	0·1
,,	2·00	,,	12·00	2·84	0·8370	0·8226	0·8514	1·75	0·1
,,	2·00	0·1N-NaOH	12·87	2·89	0·8775	0·8728	0·8822	1·20	0·1
,,	2·00	0·25N-NaOH	13·25	2·91	0·8795 †	0·8771 †	0·8819 †	1·10 †	0·25
,,	2·00	0·1N-NaOH + 0·5N-KCl	12·87	3·00	0·8660	—	—	1·12	0·6
,,	2·00	0·1N-NaOH + N-KCl	12·87	3·07	0·8643	—	—	0·89	1·1
1 : 4-$(OH)_2$	1·00	Phosphate	11·27	2·85 (av.)	0·6500	—	—	0·36	0·1
,,	1·00	,,	12·00	,,	0·6801	—	—	0·19	0·1
,,	1·00	0·1N-NaOH	12·87	,,	0·7377	—	—	0·16	0·1
,,	1·00	0·25N-NaOH	13·25	,,	0·7500	—	—	0·22	0·25
1 : 8-$(OH)_2$	1·00	Phosphate	11·27	2·85 (av.)	0·6844	—	—	0·21	0·1
,,	1·00	,,	12·00	,,	0·7204	—	—	0·33	0·1
,,	1·00	0·1N-NaOH	12·87	,,	0·7599	—	—	0·28	0·1
,,	1·00	0·25N-NaOH	13·25	,,	0·7797	—	—	0·28	0·25
2 : 6-$(OH)_2$	1·00	Borate	8·25	—	0·694	0·711	0·677	0·55	0·1
,,	1·00	,,	8·85	2·99	0·750	0·769	0·731	0·52	0·1
,,	1·00	,,	9·41	2·99	0·808	0·823	0·793	0·60	0·1
,,	1·00	,,	9·95	2·99	0·844	0·850	0·838	0·80	0·1
,,	1·00	,,	10·22	2·98	0·8544	0·8574	0·8514	0·90	0·1
,,	1·00	Phosphate	10·79	2·99	0·8850	0·8764	0·8936	1·40	0·1
,,	1·00	,,	11·27	3·01	0·9122	0·8992	0·9252	1·60	0·1
,,	1·00	,,	12·00	2·97	0·9340	0·9110	0·9570	2·45	0·1
,,	1·00	0·1N-NaOH	12·87	2·99	0·9630	0·9280	0·9980	3·90	0·1
,,	1·00	0·25N-NaOH	13·25	2·92	0·9665 †	0·9267 †	1·0063 †	4·70 †	0·25

* " Borate " and " Phosphate " represent the respective buffers. † Value corrected to $I = 0·1$.

various pH values the half-wave potential E_m, and the virtual standard redox potentials at a given pH for the first and the second one-electron reduction stage (E_1, E_2); E_m was determined for each polarogram by averaging the potentials E of the dropping-mercury electrode for pairs of points having α values equidistant from 0·5; this minimises error due to any slight departure from the theoretical symmetry of the curve about the midpoint. Then, for a given value of α and of the corresponding value of $(1 - \alpha)$, the values of $|E_m - E|$ were read off the curve and averaged. The semiquinone-formation constant

$$K = [\text{semiquinone form}]^2/[\text{oxidised form}][\text{reduced form}]$$

was then calculated from the equations (Geake, *Trans. Faraday Soc.*, 1938, **34**, 1395)

$$P = e^{2F(E_m - E)/RT}$$

$$\sqrt{K} = 2[P - 1) - (1/\alpha - 2)]/(1/\alpha - 2)\sqrt{P}$$

in which R, T, and F have their usual significance. For this purpose, Geake's tables of $2/\sqrt{P}$ and $(P - 1)$ for given values of $(E_m - E)$ were used; K values were obtained for $\alpha = 0{\cdot}1$, 0·2, 0·3, and 0·4, and the averaged value was used to calculate E_1 and E_2 from the equations

$$E_1 - E_m = E_m - E_2 = (RT/2F) \ln K$$

Table 1 also gives values of the diffusion current constant $d = \bar{i}_d/m^{\frac{2}{3}}t^{\frac{1}{6}}c$ ($\bar{i}_d$ = mean wave-height or diffusion current in μamp., and c = concentration of electroactive matter in m.-mol./l.).

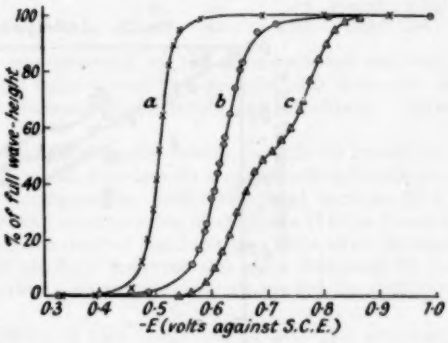


FIG. 2. *Polarograms for anthraquinone-2-sulphonic acid at 25°; I = 0·1.*

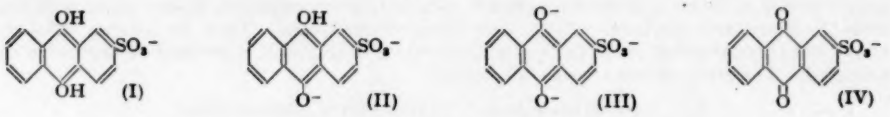
a, 3·14 × 10⁻⁴M, pH 7·82, *in water.*
b, 1·705 × 10⁻³M, pH 12·87, *in water.*
c, 0·3—3·0 × 10⁻³M, 0·1N-NaOH, *in 50% ethanol.*

Clearly, d is practically independent of pH, and, as implied by Ilkovič's equation (*Coll. Czech. Chem. Comm.*, 1934, **6**, 498), $d = 605nD^{\frac{1}{2}}$ (n = number of electrons required per molecule reduced or oxidised = 2, and D = diffusion coefficient of electroactive molecule in cm.² sec.⁻¹), also independent of concentration. However, the value differs from that (3·22) observed by Furman and Stone (*loc. cit.*), as well as from the value 2·65 calculated from their independent determination of D.

The graphs of E_m, E_1, and E_2 against pH (Fig. 3) contain linear sections with slopes which are multiples of −29·5 mv, in agreement with theory. The results of Burstein and Davidson (*loc. cit.*) for c = 0·5, temperature 30°, I (ionic strength) = 0·2, as well as those of Geake and Lemon and of Conant *et al.* (*locc. cit.*) for 25°, fit our graphs reasonably well, but not so the polarographic results of Furman and Stone (*loc. cit.*), especially where citrate, phosphate, and borate buffers were used. The cross-over point where $E_1 = E_m = E_2$, $K = 1$, occurs at pH 10·5, in exact agreement with Burstein and Davidson. Our $\sqrt{K}$–pH data (Fig. 3) are in fair accord with values calculated from the results of Burstein and Davidson, after taking into account the increase in T and I which will tend to make their K values smaller than ours. The results of Conant *et al.* lead to $\sqrt{K}$ values of *ca.* 0·5 at pH 8—10, and of 1·93 at pH 12—13, in fair agreement with Fig. 3. Bends in the E_m–pH graph give the acid pK values of the quinol as $pK_1^r = 8{\cdot}65$, $pK_2^r = 11{\cdot}05$ (cf. 7·65 and 11·05, Burstein and Davidson; 8 and 11·3, Conant *et al.*; 11·35, Furman and Stone). Thus the quinol exists in the forms $R^- = (I)$ $(6 < pH < pK_1^r)$, $R^- = (II)$ $(pK_1^r < pH < pK_2^r)$, and $R^{\equiv} = (III)$ $(pH > pK_2^r)$.

The E_1–pH graph shows distinct evidence of a bend indicating a semiquinone pK value of $pK^s = 9{\cdot}02$. Over the entire pH range examined, the semiquinone exists in only two forms.

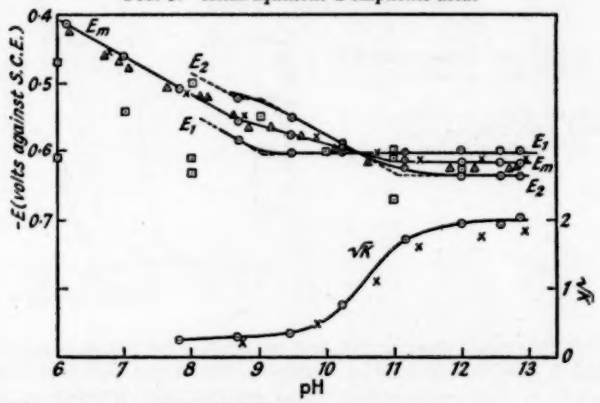
Since at pH > pK^s the E_1–pH graph is horizontal, formation of semiquinone from quinone [which exists only in the form $T^- = (IV)$] involves no protons, and is thus represented by



$T^- + e \longrightarrow S^-$. Hence semiquinone exists as S^- (= V) at pH > pK^s, and as S^- (= VI) at pH < pK^s. Since S^- lacks the possibility of equivalent resonance present in S^-, the value of K falls rapidly as pH falls (cf. Fig. 3).

The E_2–pH graph shows the expected bend at pH = pK_2^r. At pH > pK_2^r the second reduction step is clearly $S^- + e \longrightarrow R^{\equiv}$, and at pH's between p$K^s$ and pK_2^r it is $S^- + e + H^+ \longrightarrow R^-$. For pH's between p$K_1^r$ and pK^s it should be $S^- + e \longrightarrow R^-$

FIG. 3. *Anthraquinone 2-sulphonic acid.*



⊙ *This work*: 2×10^{-3}M *in* H_2O, 25°; $I = 0{\cdot}1$.
△ E_m, *Conant* et al., *in water*, 25°.
× E_m *and* $\sqrt{R}$, *Burstein and Davidson*, 5×10^{-4}M, *in water*, 30°; $I = 0{\cdot}2$.
⊡ E_m, *Furman and Stone*, 10^{-3}M *in* 1% EtOH, 24°.

corresponding to a zero E_2–pH slope. Again, for pH < pK_1^r the process must be $T^- + e + H^+ \longrightarrow S^-$, corresponding to a 59 mv slope. Thus the E_2–pH graph should have bends at pK_1^r and pK^s, and the sparse data in this pH region are not in disagreement with this, as shown in Fig. 3.

With the above assumptions regarding the various ionic forms present, the equations of the E_m–pH, E_1–pH, and E_2–pH curves may be shown by well-known methods (cf. Kaye and Stonehill, *locc. cit.*) to be as follows:

$$E_m = (E_m^\circ - 0{\cdot}0295 \log K_1^r K_2^r) + 0{\cdot}0295 \log (K_1^r K_2^r + K_1[H^+] + [H^+]^2)$$

$$E_1 = (E_1^\circ - 0{\cdot}059 \log K^s) + 0{\cdot}059 \log ([H^+] + K^s)$$

$$E_2 = \left(E_2^\circ - 0{\cdot}059 \log \frac{K_1^r K_2^r}{K^s}\right) + 0{\cdot}059 \log \frac{K_1^r K_2^r + K_1^r[H^+] + [H^+]^2}{[H^+] + K^s}$$

where E_m°, E_1°, and E_2° are constants equal to the values of E_m, E_1, and E_2 respectively at pH > pK_2^r, in which region the three graphs are all horizontal and ionisation is complete for all three oxidation levels. We find $E_m^\circ = -0{\cdot}618$ v, and therefore $E_m = -0{\cdot}047$ and $-0{\cdot}618$ v

at pH = 0 and pH > pK_2' respectively, in agreement with the values −0·051 and −0·621 v obtained from the data of Conant *et al.* (*loc. cit.*), after correction to the saturated calomel electrode standard ($E^{25°}_{\text{S.C.E.}}$ = 0·238 v).

The effect of including 50% by volume of ethanol in the solvent is shown in Fig. 2*c*, which is a composite polarogram for five different concentrations of the quinone with varying extents of reduction before being polarographed. The wave, which is slightly unsymmetrical about the centre, is two-stepped, indicating a high K value (see Table 2). A similar but smaller increase in K was observed by Burstein and Davidson (*loc. cit.*) when 50% methanol was used as solvent. Another effect of the inclusion of ethanol was the decrease of d (Table 2).

TABLE 2. *Results for aqueous-ethanolic solutions* 0·1N *in* NaOH (I = 0·1)

Substituents	c	EtOH, vol. %	d	$-E_m$ (v)	$\sqrt{K}$	Substituents	c	EtOH, vol. %	d	$-E_m$ (v)	$\sqrt{K}$
1-SO_3H ...	0·40	0	3·00	0·6774	0·47	2-SO_3H ...	2·00	0	3·00	0·618	2·02
,, ...	1·00	0	2·97	0·6748	0·39	,, ...	0·3—3·0	50	1·94	0·7115	15·0
,, ...	0·55	50	1·78	0·7127	0·44						
,, ...	5·30	50	1·82	0·7103	0·33	1-OH	2·29	0	2·86	0·7098	0·35
1 : 2-$(OH)_2$	2·00	0	2·89	0·8775	1·20	,, ...	2·33	50	1·81	0·7711	0·72
,,	2·00	5	2·75	0·8863	1·65	2-OH	1·00	0	3·08	0·8258	3·32
,,	2·00	10	2·26	0·8948	1·81	,, ...	1·00	6	2·84	0·8320	4·05
,,	2·00	25	1·76	0·9153	2·50	,, ...	1·00	12·5	2·55	0·8375	4·82
,,	2·00	50	1·40	0·9521	2·65	,, ...	1·00	20	2·35	0·8518	5·15
2 : 6-$(OH)_2$	1·00	0	2·99	0·9630	3·90	,, ...	1·00	30	2·15	0·8752	5·41
,,	1·00	50	1·71	1·142	6·2	,, ...	1·00	40	1·97	0·8978	5·17
						,, ...	1·00	50	1·90	0·9132	4·84
						,, ...	1·00	66	1·93	0·9326	4·41

Visual evidence of semiquinone formation was provided by the colour change sequence, colourless ⟶ amber ⟶ red, observed during reduction of the quinone with dithionite in strongly alkaline solution, confirming previous observations (Burstein and Davidson; Geake and Lemon, *locc. cit.*).

(3) *Anthraquinone-1-sulphonic acid.* This was studied only briefly, mainly to investigate the possibility that the large sulphonate group would give rise to an *ortho*-effect in which a carbonyl group is strained out of the coplanar configuration, with consequent decrease in K. The results in aqueous and 50% ethanolic 0·1N-alkali as supporting electrolytes (Tables 1 and 2) exhibit the following points of contrast with the behaviour of the 2-isomer: K is much smaller, and is practically independent of the presence of alcohol; however, d is again decreased by the presence of alcohol. The colour sequence, colourless ⟶ orange ⟶ orange-red, on reduction in alkali confirms the presence of semiquinone.

(4) *1-Hydroxyanthraquinone.* The low solubility of this compound at pH <12, especially in aqueous solvents, limited the work on it. Results obtained with partly pre-reduced solutions are given in Tables 1 and 2. K is very small in aqueous solutions. The presence of 50% of ethanol causes a large increase, although, since E_m still varies with pH in the region investigated, indicating incomplete ionisation, the effect of the alcohol may be due partly to the pH shift and also to the change in acid dissociation constant caused by its inclusion. The decrease in K in going from 0·1 to 0·25N-aqueous alkali may be due to the effect of the increasing ionic strength opposing and overbalancing the expected increase due to rise of pH. The presence of alcohol again decreases d. Colour changes observed during reduction (red ⟶ orange-red ⟶ orange in water; red ⟶ deep red-brown ⟶ orange in 50% alcohol) indicate little semiquinone formation in water, but appreciable formation of greenish semiquinone in 50% alcohol.

(5) *2-Hydroxyanthraquinone.* This is sufficiently soluble at pH >8 to permit investigation over a wide pH range. However, the leuco-compound tautomerises in aqueous solutions at pH <12. Therefore, although values of K and E_m are independent of whether the compound is in the oxidised or the reduced form at any pH provided that time is allowed for equilibration of the tautomerism before polarography, the value of d is strongly dependent on pH for the reduced form (Gill and Stonehill, *J.*, 1952, 1857). For the oxidised form, d is independent of pH, and thus the present results were obtained exclusively for this form. In Fig. 4 are plotted the values of E_m, E_1, E_2 and $\sqrt{K}$ against pH. From the bends in the E_m–pH graph the values of three acid pK values for the quinol are determined as $pK_1' = 8·7$, $pK_2' = 10·05$, $pK_3' = 12·60$. The intersection corresponding to pK_1' is somewhat uncertain, and was determined by drawing through the point at pH 8·22 a straight line with the theoretical slope of −88 mv for a $3H^+$–$2e$ reduction, to meet the neighbouring linear portion of the graph. Apart from the bend at pK_1' (E_m–pH graph), which constant may, by comparison with the value $pK^I = 7·62$ for the

quinone at 18° (Heilbron, "Dictionary of Organic Chemistry," Eyre and Spottiswoode, 1936), be associated with the ionisation of the quinol to the analogue of (I), the graphs of Fig. 4 are similar to the corresponding ones for anthraquinone-2-sulphonic acid, and may be similarly interpreted. By familiar methods we then deduce the equations

$$E_m = \left(E_m^\circ - 0{\cdot}0295 \log \frac{K_1^r K_2^r K_3^r}{K^i}\right) + 0{\cdot}0295 \log \frac{K_1^r K_2^r K_3^r + K_1^r K_2^r [H^+] + K_1^r [H^+]^2 + [H^+]^3}{K^i + [H^+]}$$

$$E_1 = \left(E_1^\circ - 0{\cdot}059 \log \frac{K^s}{K^i}\right) + 0{\cdot}059 \log \frac{K^s + [H^+]}{K^i + [H^+]}$$

$$E_2 = \left(E_2^\circ - 0{\cdot}059 \log \frac{K_1^r K_2^r K_3^r}{K^s}\right) + 0{\cdot}059 \log \frac{K_1^r K_2^r K_3^r + K_1^r K_2^r [H^+] + K_1^r [H^+]^2 + [H^+]^3}{K^s + [H^+]}$$

where E_m°, E_1°, and E_2° (values of E_m, E_1, and E_2 at pH $> pK_3^r$) are respectively $-0{\cdot}828$, $-0{\cdot}797$, and $-0{\cdot}858$v, $pK^i \approx 8$, $pK^s = 10{\cdot}3$.

The maximum value of $\sqrt{K}$ (*ca.* 3·55), observed at extreme alkalinities, is roughly midway between the corresponding values for anthraquinone (2·6) and for 2 : 6-dihydroxyanthraquinone (5·00). At the lowest pH values studied, $\sqrt{K}$ tends to a non-zero limit of *ca.* 0·3; this is probably not due to experimental error, but is a real lower limit, since it was obtained in several replicate experiments, and is similar to results obtained with other compounds examined.

Fig. 5 shows the effect of progressively increasing the volume percentage of ethanol in the

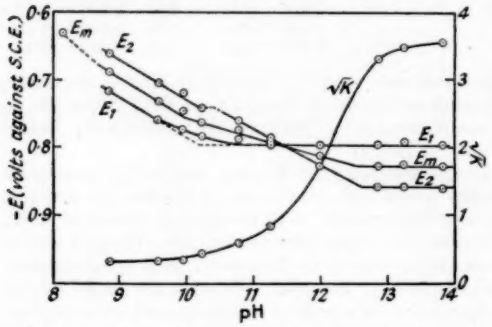


FIG. 4. *2-Hydroxyanthraquinone:* 1×10^{-3}M *in* H_2O, 25°; $I = 0{\cdot}1$.

solvent on the redox and polarographic characteristics of 2-hydroxyanthraquinone in 0·1N-sodium hydroxide. $\sqrt{K}$ exhibits a maximum, whereas for anthraquinone-2-sulphonic acid it increases steadily (Burstein and Davidson, *loc. cit.*). The maximum is probably due to decreasing ionisation of the hydroxy-compound with rise in ethanol content, causing diminution in K which eventually overbalances the usual increase due to the effect of alcohol on the purely redox equilibrium. Half-wave potentials E_m, obtained by neglecting alcohol–water junction potentials (see Table 2), steadily become more negative with increasing ethanol content, owing to the effect of solvent change on the purely redox equilibrium, on which is superimposed a smaller opposite shift to more positive values, due to decreasing ionisation of the leuco-compound. The value of d falls initially as alcohol content increases, but then remains practically constant for >45% of alcohol. These effects are due entirely to variation in D; ionisation cannot be concerned, since D is virtually identical for the quinone, semiquinone, and quinol at all ionisation levels, association or polymerisation being assumed to be absent.

The effect on the redox-polarographic behaviour in 0·1N-aqueous sodium hydroxide of increasing the ionic strength by adding potassium chloride is shown in Fig. 6 and Table 1. While d remains practically constant, $\sqrt{K}$ decreases and E_m becomes progressively more positive. These changes are due mainly to the effect of varying ionic strength on the purely redox equilibrium, but there is also a small contribution from the secondary salt-effect on the acid–base ionisation of the quinol, since in 0·1N-alkali the ionisation is not quite complete.

The colour sequence, red ⟶ dark brown ⟶ green ⟶ yellow, observed during reduction at higher pH values visually confirms semiquinone formation.

(6) 1 : 2-*Dihydroxyanthraquinone* (*alizarin*). The variation of E_m, E_1, E_2, $\sqrt{K}$, and d with pH is shown in Table 1 and Fig. 7. The maximum in $\sqrt{K}$ plotted against pH is unique amongst the compounds studied; the small decrease in $\sqrt{K}$ at pH >12 was confirmed by several

replicate experiments. Attempts to investigate solutions in N-alkali were unsuccessful, because of erratic galvanometer deflections, probably caused by salting-out, which also occurred to some extent in experiments with added potassium chloride. Solutions left overnight usually flocculated, and coated the mercury pool with a yellow film (possibly a lake), insoluble in dilute alkali but removed by acid followed by acetone. Because of insufficient data, the slopes and positions of bends in the E_m, E_1, and E_2 graphs are difficult to determine, and only a very speculative assignment of pK values, indicated in Fig. 7, can be made; it is particularly difficult to explain the course of the E_2 graph, and the large change of slope of the E_m graph near pH 11·6.

Increase in ionic strength, by addition of potassium chloride to solutions in 0·1N-aqueous alkali, causes the usual fall in $\sqrt{K}$ and shift of E_m to more positive values (Table 1), and slightly increases d. The inclusion of ethanol in solutions in 0·1N-alkali increases $\sqrt{K}$, makes E_m more

FIG. 5. *2-Hydroxyanthraquinone in* 0·1N-NaOH *at* 25°. *Effect of* EtOH *on* $\sqrt{K}$ *and* d.

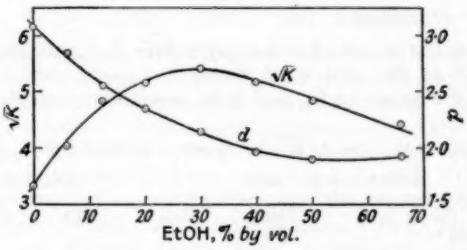


FIG. 6. *2-Hydroxyanthraquinone in* 0·1N-NaOH at 25°. *Effect of* KCl *on* $\sqrt{K}$ *and* E_m.

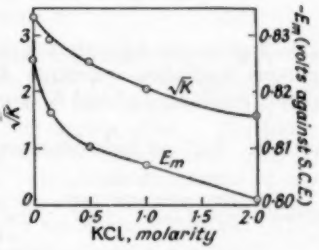


FIG. 7. 1 : 2-*Dihydroxyanthraquinone.* 2×10^{-3}M, *in* H_2O *at* 25°; $I = 0·1$.

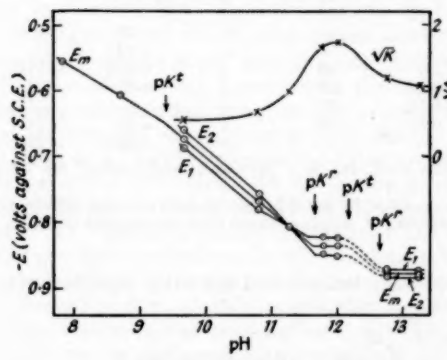
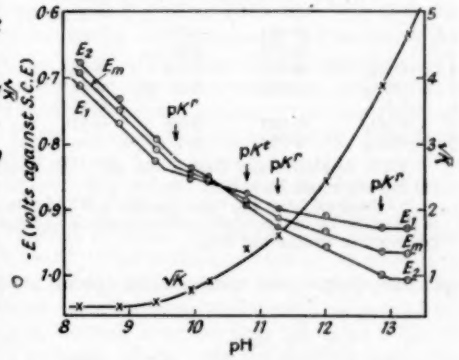


FIG. 8. 2 : 6-*Dihydroxyanthraquinone.* 10^{-3}M, *in* H_2O *at* 25°; $I = 0·1$.



negative (liquid-junction potentials neglected), and decreases d considerably (Table 2). However, since for some of the species involved ionisation is not complete in 0·1N-alkali, the effect of both potassium chloride and alcohol on $\sqrt{K}$ and E_m is composite, being due partly to the effect on the purely redox equilibrium, and partly to the effect on acid–base ionisation equilibria.

Confirming the results of Appleton and Geake (*Trans. Faraday Soc.*, 1941, **37**, 45), the colour change, violet, ⟶ olive-green ⟶ orange, observed during reduction at pH ≈12 demonstrates the formation of semiquinone.

(7) 1 : 4- *and* 1 : 8-*Dihydroxyanthraquinones.* These have been titrated potentiometrically by Appleton and Geake (*loc. cit.*), but only in sodium hydroxide solutions in water and 50% aqueous pyridine at 50°. At pH <11·27, the insolubility of these compounds rendered polarography impossible, and even at pH 11·27 results were rather erratic. Results are given in Table 1, and indicate incompleteness of ionisation even at pH 13·25; hence the effects of alcohol in the solvent were not studied, since considerable alteration in acid–base ionisation would interfere. The colour changes observed during reduction (red-violet to orange for the

1 : 4-isomer; red ⟶ orange ⟶ yellow for the 1 : 8-isomer) confirm the virtual absence of semiquinone formation indicated by the low $\sqrt{K}$ values.

(8) 2 : 6-*Dihydroxyanthraquinone.* As with 2-hydroxyanthraquinone, tautomerism of the anthraquinol (Gill and Stonehill, *loc. cit.*) here necessitated working with only the quinone in order to obtain time-independent d values. Results are given in Table 1 and Fig. 8. Again, only a very tentative assignment of pK values corresponding to bends in the E_m, E_1, and E_2 against pH graphs has been made in Fig. 8. Since the anthraquinol is not quite completely ionised even at pH 13·25, $\sqrt{K}$ shows no signs of levelling off to a constant maximum at this pH. For the same reason, only a single determination of the effect of alcohol on E_m and $\sqrt{K}$ was made (Table 2); the decrease in ionisation due to the presence of alcohol makes a considerable contribution to the observed increase in $\sqrt{K}$ and the shift of E_m to a more negative value. The usual decrease in d due to alcohol also occurs.

The colour change during reduction in alkali (red ⟶ dark red-brown ⟶ yellow) confirms the extensive formation of semiquinone indicated by the relatively high $\sqrt{K}$ values at high pH.

Discussion

Table 3 gives for aqueous solution the standard redox potentials $E_m°$ and standard semiquinone formation constants $K°$ at 25° and ionic strength $I = 0·1$, for all the compounds studied; $E_m°$ and $K°$ are the values of E_m and K for conditions such that the

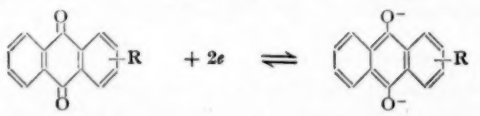
Table 3. $E_m°$ *(on hydrogen-electrode scale) and* $\sqrt{K°}$ *for aqueous solutions* ($I = 0·1$)

	This work (25°):		Potentiometric data:				$\Delta E_m°$ (mv):	
Substituent	$-E_m°$ (v)	$\sqrt{K°}$	$-E°$ (v)	$\sqrt{K}$	Temp.	Ref.[a]	Obs.	Calc.
None	—	—	0·444 [c]	—	25°	1	—	—
			0·454 [b]	2·6 [b]	50	1		
1-SO_3H	0·432	0·45	0·444	0·23	25	2	+12	—
2-SO_3H	0·374	1·94	0·381	1·92	25	2	+70	—
			0·374	1·76	25	3		
			0·379	1·83	30	4		
1-OH	0·481	0·22	—	—	—	—	−37	—
2-OH	0·582	3·6	—	—	—	—	−137	—
1 : 2-$(OH)_2$ ...	0·637	1·14	0·624	1·7	20	1	−193	−174
1 : 4-$(OH)_2$ ...	0·506	0·2	0·485	0·05	50	1	−62	−74
1 : 5-$(OH)_2$ ...	—	—	0·478	0·33	50	1	—	—
1 : 8-$(OH)_2$ ...	0·536	0·28	0·578	0·31	50	1	−92	−74
2 : 6-$(OH)_2$ ...	0·724	4·7	—	—	—	—	−280	−274

[a] (1) Appleton and Geake, *loc. cit.*; (2) Conant *et al.*, *loc. cit.*; (3) Geake and Lemon, *loc. cit.*; (4) Burstein and Davidson, *loc. cit.*

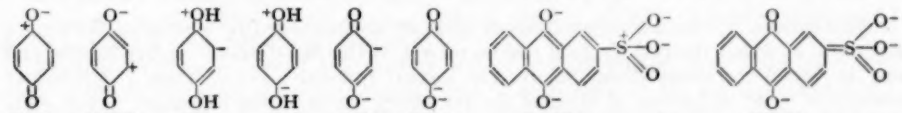
[c] Obtained from the value for the 2-SO_3H compound at 25° by subtracting 70 mv, which difference is stated to be independent of temperature and medium. [b] Approx. value from incomplete titration; not used in evaluating $\Delta E_m°$.

quinone, quinol, and semiquinone species are all fully ionised, and the redox equilibrium is



For several of the compounds, ionisation is complete in 0·1N-sodium hydroxide, and the values of E_m and K in this solvent may be taken as $E_m°$ and $K°$, respectively. Where ionisation is not complete in 0·1N-alkali (indicated by E_m still varying as pH increases), $E_m°$ and $K°$ are estimated by correcting E_m and K values obtained in more concentrated alkali (in which complete ionisation may be assumed) for the variation with I, using for this purpose results obtained with added potassium chloride. For 1 : 4- and 1 : 8-dihydroxyanthraquinones, ionisation was not complete even in N-alkali, and thus the estimated (extrapolated) values of $E_m°$ and $K°$ are less accurate. Some values taken or calculated from earlier potentiometric data in the literature are included in Table 3 for comparison. Agreement with present values is reasonable, except for 1 : 4- and 1 : 8-dihydroxyanthraquinones, for which ionisation is incomplete.

Effect of Substituents on $E_m°$.—The observed shifts $\Delta E_m°$ are listed in Table 3, col. 8. For disubstitution, the observed shifts agree in general with those calculated from simple additivity (Table 3, last column). To explain the results, we assume (cf. Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall Inc., 1941, pp. 305, 315) that for a series of anthraquinones, $\Delta S°$ for the process ox. $+ 2e \longrightarrow$ red. is practically constant, so that variations of $E_m° = -\Delta G°/2F$ measure variations in $-\Delta H° = -H°_{red.} + H°_{ox.}$, or in (resonance energy of "red.") − (resonance energy of "ox.") (Evans, *Trans. Faraday Soc.*, 1936, **42**, 113; Evans and De Heer, *Quart. Reviews*, 1950, **4**, 104). The chief ionic resonance in quinones throws a positive charge into the ring, as in (VII) and (VIII), so that



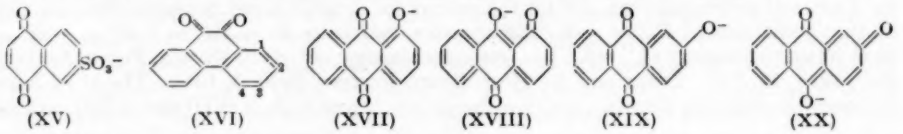
(VII) (VIII) (IX) (X) (XI) (XII) (XIII) (XIV)

any group such as OH, which by induction or resonance assists the ring to accommodate this positive charge, will stabilise the quinone and thus make $E_m°$ more negative. (In the terminology of Evans and de Heer, "induction" becomes the inductive effects on σ and on π electrons; "resonance" corresponds to the conjugation effect.) Similarly, ionic resonance introduces a negative charge into the ring for un-ionised quinols (IX, X), and with even greater effect for ionised quinols (XI, XII) because of the absence of opposite-charge separation. Thus quinols are stabilised by the electron-attracting SO_3^- substituent, which acts by induction and perhaps also by resonance of the type (XIII) $\longleftrightarrow$ (XIV) (cf. Bryson, *Trans. Faraday Soc.*, 1951, **47**, 528), thereby rendering $E_m°$ more positive.

The smallness of the positive $\Delta E_m°$ for anthraquinone-1-sulphonic acid is probably due to an "*ortho*-effect" caused by steric hindrance, which pushes both the $=O$ and the $-SO_3^-$ group out of the ring plane, thereby inhibiting any resonance not only of the carbonyl oxygen atom with the ring (hence the small $\sqrt{K}$ value for the semiquinone), but also of the $-SO_3^-$ group with the ring; thus only the small inductive effect of the latter group remains, and even this is opposed by the effect on $E_m°$ due to the displacement of the carbonyl oxygen from the ring plane. In the 2-sulphonic acid, resonance of the type (XIII) $\longleftrightarrow$ (XIV) reinforces the inductive effect, giving $\Delta E_m° = +70$ mv, almost exactly equal to the $\Delta E°$ value $+75$ mv for the correspondingly substituted 1 : 4-naphthaquinone (XV) in water (Fieser and Fieser, *J. Amer. Chem. Soc.*, 1935, **57**, 491). Introduction of an $-SO_3^-$ group in phenanthraquinone (XVI) leads to a $\Delta E°$ of about $+25$ mv, almost independent of position (*i.e.*, for positions 1, 2, and 3), thus indicating little or no resonance effect (Fieser, *J. Amer. Chem. Soc.*, 1929, **51**, 3101); this result, although found for solutions in 50% alcohol, is probably applicable to aqueous solutions also, as judged by other results of the same author. Accordingly, we may suppose that the total $\Delta E_m°$ of $+70$ mv for anthraquinone-2-sulphonic acid is made up of $+25$ mv for the inductive effect, and $+45$ mv for the resonance effect.

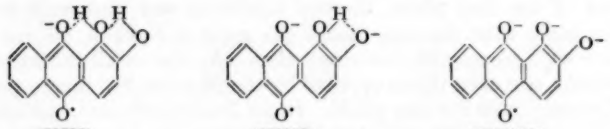
The $\Delta E°$ values of -1 and 0 mv respectively for 2- and 4-hydroxyphenanthraquinones (Fieser, *loc. cit.*), for which resonance stabilisation of the quinone by the substituent is impossible, show that the inductive effect of OH on $E°$ or on $E_m°$ is practically nil. If, however, OH is replaced by $-O^-$, as in the present results, a definite inductive effect is to be expected, which by comparison with that of $-SO_3^-$ is probably about -20 mv, although it may vary with position in the ring. Since $\Delta E_m°$ is -37 mv for ionised 1-hydroxyanthraquinone, about -17 mv of this must be due mainly to resonance of the form (XVII) $\longleftrightarrow$ (XVIII), but also partly to repulsion of the ionised quinol oxygen by the nearby substituent $-O^-$ group, causing destabilisation of the quinol. For ionised 2-hydroxyanthraquinone, in addition to an inductive $\Delta E_m°$ of -20 mv, there is a large effect due to *para*-resonance (XIX) $\longleftrightarrow$ (XX), which is clearly of greater importance here than in the un-ionised molecule (OH instead of $-O^-$ in the 2-position), for which a separation of opposite charges would be required. For un-ionised 1- and 3-hydroxy-

phenanthraquinones, ΔE° is −50 and −53 mv, respectively (Fieser, *loc. cit.*), entirely due to resonance, since we have seen that inductive effects are negligible. The rough estimate that *para*-resonance of the ionised hydroxy-group contributes −120 mv of the total ΔE_m° observed (−137 mv) for ionised 2-hydroxyanthraquinone is therefore reasonable.



(XV) (XVI) (XVII) (XVIII) (XIX) (XX)

Semiquinone Formation.—Semiquinone radicals are stabilised by resonance between a structure in which the odd electron resides on one of the two quinone oxygen atoms, and one in which it resides either (*a*) on the second quinone oxygen atom ("equivalent resonance"), or (*b*) on one or other of the remaining atoms in the molecule. Type (*a*) is far the more important, and where it is possible, *e.g.*, in the fully ionised semiquinones of anthraquinone and its 2-substituted derivatives, high K values result. A substituent in the 1-position interferes with this type of resonance, by steric effects ($-SO_3^-$), hydrogen bonding (−OH), or mutual repulsion of negative charges ($-O^-$), resulting in low K values characteristic of the weaker type (*b*) resonance. At lower pH's, where a proton adds to one of the quinone oxygen atoms, type (*a*) resonance is inhibited even for compounds for which it occurs at higher pH's, giving low but non-zero K values corresponding to type (*b*) resonance. The unusual form of the $\sqrt{K}$–pH curve for 1 : 2-dihydroxyanthraquinone (Fig. 7) may be explained as due to the normal initial rise in K with pH increase because of increasing ionisation of the quinol hydroxy-groups, which, at pH's high enough to ionise both substituent hydroxy-groups, is counteracted by mutual repulsion of negative charges ($-O^-$) causing a fall in K. The ionisation sequence for the semiquinone is probably (XXI) ⟶ (XXII) ⟶ (XXIII).



(XXI) (XXII) (XXIII)

Effects of Change of Solvent.—Burstein and Davidson (*loc. cit.*) found that, for fully ionised sodium anthraquinone-2-sulphonate in 0·1N-sodium hydroxide at 30°, inclusion in the aqueous solvent of up to 30% of methanol, pyridine, or dioxan caused variation in K according to $\log K = A/\varepsilon$ (ε = dielectric constant), in qualitative agreement with Born's equation (*Z. Physik*, 1920, **1**, 45) for the variation of activity coefficients with ε, but with the constant A much greater than the theoretical value. In the present work, the only compound studied which is completely ionised in 0·1N-alkali, apart from the 2-sulphonic acid, is 2-hydroxyanthraquinone, and even this becomes incompletely ionised on introduction of ethanol; the use of higher alkali concentrations to prevent this would cause complicating effects due to increased ionic strength. For this compound, K rises initially as the alcohol content or $1/\varepsilon$ increases, but eventually the effect of repression of ionisation preponderates, causing a fall in K. The initial rise in K is also found with the 2-sulphonic acid, the 1-hydroxy- and the 1 : 2-dihydroxy-derivative, but not with the 1-sulphonic acid.

The introduction of ethanol renders E_m more negative for all the compounds studied, and also reduces d progressively up to about 50% alcohol. For 2-hydroxyanthraquinone, for which the most complete study of the effect of alcohol was made, d falls until about 45% of alcohol is present, and then remains practically constant up to 70% alcohol content.

Effects of increasing Ionic Strength.—In all cases studied, addition of potassium chloride at constant pH (0·1N-sodium hydroxide in water) makes E_m more positive, does not affect d, and diminishes K. Although salt effects on the incomplete ionisation of weakly

acid hydroxyl groups may cause complications, the effects on E_m and K are qualitatively in agreement with deductions from the Debye–Hückel equation for activity coefficients of ions, if it is remembered that E_m and K in this paper refer to equations in which concentrations and not activities of quinone, semiquinone, and quinol species are used.

Diffusion-current Constants.—There is poor agreement between present d values and those of Furman and Stone (*loc. cit.*); *e.g.*, for the 1- and 2-sulphonic acid and 1 : 2-dihydroxy-derivative, respectively, the values we obtain (Furman and Stone's values in parentheses) are 2·99 (3·60), 3·02 (3·22), and 2·88 (3·09). In view of the preceding section of this paper, the discrepancy is not due to differences of ionic strength in the two investigations; neither is it because our results relate to aqueous solvent and those of Furman and Stone to 1% ethanol, since any slight effect of including 1% of ethanol would be to decrease d, thus increasing the discrepancy.

Furman and Stone suggest that borate and phosphate buffers form complexes with some of the substituted anthraquinones as well as with some of the corresponding semiquinones, thus shifting E_m to more negative values than apply when other buffers are used at the same pH. A similar explanation is suggested by Elving, Komyathy, Van Atta, Tang, and Rosenthal (*Analyt. Chem.*, 1951, **23**, 1218) to account for their observation that both d and E_m may be altered for α-bromo-*n* butyric acid if the concentration, but not the nature, of the buffer components is changed, even if pH and I are kept constant; variation of I alone scarcely affected d.

Since the concentration ratio of buffer to anthraquinone derivative was roughly the same (about 100 : 1) in the present work and in that of Furman and Stone, the discrepancy in d values cannot be due to different extents of complexing by the buffer, with consequent increase in molecular size of electroactive species and decrease in d to different extents. The large discrepancies in E_m (cf. Fig. 3) are also difficult to explain, and in view of the agreement between our results and earlier potentiometric data, the results of Furman and Stone must be regarded with some doubt.

TECHNICAL COLLEGE, BRADFORD, YORKS.
MEDWAY TECHNICAL COLLEGE, GILLINGHAM, KENT. [*Received, December 13th*, 1951.]

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341. *A Polarographic Investigation of the Tautomerism of 2-Hydroxy- and 2 : 6-Dihydroxy-anthraquinol.*

By R. GILL and H. I. STONEHILL.

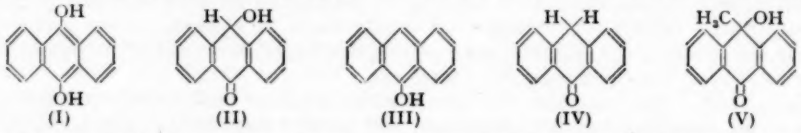
Over a certain pH range for each, 2-hydroxy- and 2 : 6-dihydroxy-anthraquinol give polarographic oxidation waves which decrease in height with time. This is shown to be due to reversible tautomerisation to the corresponding oxanthrols, which are polarographically reducible at highly negative potentials. The tautomeric equilibrium point varies with pH, maximum equilibrium conversion into the oxanthrol occurring at pH 8·85—9·59 for the 2-hydroxy-compound. From this it is deduced that the particular state of ionisation of the quinol responsible for the tautomerisation is that in which only one of the three hydroxy-groups is ionised. The tautomeric oxanthrol is stabilised relative to the anthraquinol by ionic *para*-resonance, which is possible only if an ionised 2-hydroxy-group is present. In 1 : 2-dihydroxyanthraquinol, the 1-hydroxy-group prevents tautomerisation by causing hydrogen bonding in the quinol and steric hindrance in the oxanthrol.

The velocity of the tautomerisation is in accordance with the assumption of first-order kinetics for the forward and the reverse reaction.

DURING the investigation reported in the preceding paper, in which all experimental details are given, it was observed that 2-hydroxy- and 2 : 6-dihydroxy-anthraquinone, alone amongst the compounds studied, gave in the leuco-form, over a certain pH range for each, anodic diffusion currents (wave-heights) which decreased with time to non-zero equilibrium values, although the position and shape of the polarographic wave (*i.e.*, values

of half-wave potential E_m and semiquinone formation constant K) remained unchanged. In the oxidised (quinone) form, the compounds gave corresponding cathodic waves with height independent of time. At the same time as the normal anodic wave for the anthraquinols diminished, a new cathodic wave appeared at much more negative potentials, which increased in height at approximately the same rate as the decrease of the normal wave, reaching a maximum equilibrium value after about 40 minutes at room temperature.

The tautomerism of anthraquinol (I) $\rightleftharpoons$ oxanthranol (II), and the similar behaviour of anthranol (III) $\rightleftharpoons$ anthrone (IV), are well known. We now show that the abnormal



polarography of 2-hydroxyanthraquinol, and presumably also of 2 : 6-dihydroxyanthraquinol, is due to tautomerisation similar to (I) $\rightleftharpoons$ (II) occurring in a particular state of ionisation, the tautomer analogous to (II) undergoing reduction at highly negative potentials to the analogue of (IV).

Results.—Figs. 1 and 2 show typical polarograms for the two anthraquinones in various states of reduction, and refer to solutions which were equilibrated before being polarographed,

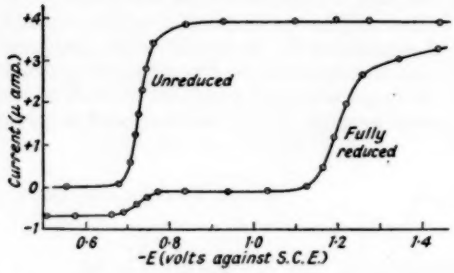


FIG. 1. *Polarograms for* $9{\cdot}47 \times 10^{-4}$M-*2-hydroxyanthraquinone :* pH 9·59, 25°.

by waiting for 1 hour after adding any dithionite (hydrosulphite) required. Table 1 shows that the unreduced 2-hydroxyanthraquinone does not undergo conversion at any pH investigated, whereas the anthraquinol is converted to an extent which at equilibrium varies with pH. That the conversion reaches an equilibrium follows from the fact that the normal anodic wave, due to unconverted anthraquinol, never disappears entirely, as shown in Table 1 and also in cols. 1—3 of Table 2.

On reduction of 2-hydroxyanthraquinone with dithionite at pH $<$ *ca.* 11, the colour

TABLE 1. *Equilibrium diffusion current constants for 2-hydroxyanthra-quinone and -quinol in aqueous buffers at* 25°.

Buffer	N-NaOH	0·1N-NaOH	Phosphate	Phosphate	Borate	Borate
Ionic strength	1·0	0·1	0·1	0·1	0·1	0·1
pH	13·79	12·87	12·00	11·27	9·59	8·85
Diffusion current constant { Quinone	3·00	3·08	3·03	3·12	3·09	3·04
Diffusion current constant { Quinol ...	3·01	2·96	2·66	1·31	0·61	0·58

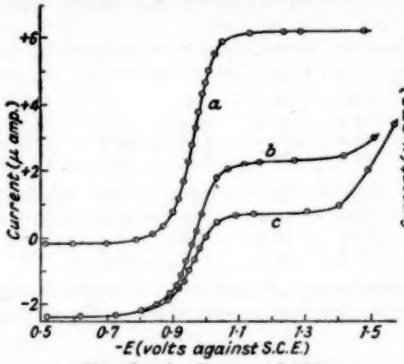
TABLE 2. *Equilibrium concentrations of various species in* $1{\cdot}415 \times 10^{-3}$M-*2-hydroxyanthraquinone in different states of reduction.*

In aqueous phosphate buffer, pH 11·27, ionic strength 0·1, at 25°. $E_m = -0{\cdot}7910$ v (S.C.E.), $\sqrt{K} = 0{\cdot}86$, $m = 0{\cdot}924$ mg./sec., $t = 4{\cdot}68$ sec.

State of solution	Wave height (μamp.): cathodic	anodic	$-E$ (S.C.E.) at zero current	$r+s+t$	y	r	s	y/r	y/s
Unreduced	5·41	0·00	—	5·41	0·00	—	—	—	—
Partly reduced	1·27	1·84	0·7952	3·11	2·30	1·27	0·927	1·81	2·48
Further reduced	0·33	2·04	0·8245	2·37	3·04	1·81	0·423	1·68	7·19

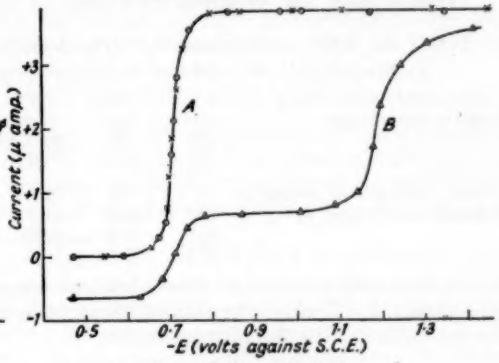
changes from red through orange to yellow, and remains yellow as the anthraquinol wave-height decreases. Upon reoxidation of the equilibrated anthraquinol solution by bubbling air through it, the red colour returns slowly (1—2 hours), in contrast with the almost instantaneous reoxidation observed at pH 13, or with the other compounds with normal polarographic behaviour studied in the preceding paper. That the reoxidation gives a

FIG. 2. *Polarograms for* $1{\cdot}8 \times 10^{-3}$M-2 : 6-*dihydroxyanthraquinone :* pH 12·87, 25°.



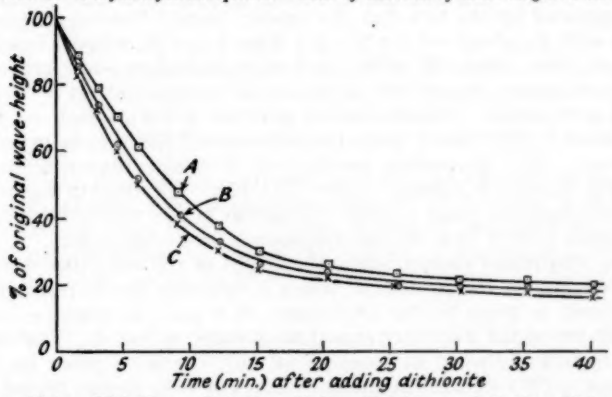
a, *Unreduced :* $E_m = -0{\cdot}964$ v.
b, *Half reduced :* $E_m = -963$ v.
c, *Further reduced :* $E_m = -959$ v.

FIG. 3. *Polarograms for* $1{\cdot}286 \times 10^{-3}$M-2-*hydroxyanthraquinone :* pH 9·34, 15°.



—⊙— *Before reduction.*
—△— *After partial reduction.*
—×— *After reoxidation.*

FIG. 4. 2-*Hydroxyanthraquinol. Rate of decrease of wave height at* 25°.



A, $2{\cdot}38 \times 10^{-4}$M, pH 8·85. *B*, $1{\cdot}48 \times 10^{-3}$M, pH 8·85. *C*, $9{\cdot}46 \times 10^{-4}$M, pH 9·59.

quantitative yield of 2-hydroxyanthraquinone is shown by the following. A $1{\cdot}286 \times 10^{-3}$M-solution of the quinone at pH 9·34 and 15° gave a cathodic wave at about −0·7 v against the saturated calomel electrode (S.C.E.), of height 3·85 μamp. (Fig. 3, *A*). This solution was part-reduced with dithionite, and after time had been allowed for equilibration gave a diminished wave at the same potential, of height 1·36 μamp. (Fig. 3, *B*). The solution was reoxidised with an air stream, and after 12 hours' standing and then removal of excess of air with nitrogen, it gave a polarogram almost identical with the original one, with wave-height 3·88 μamp.

Fig. 4 gives some typical results illustrating the effects of change of concentration and of pH upon the rate of decrease of wave-height for 2-hydroxyanthraquinol with time after reduction of the anthraquinone. It is clear from these and other similar results that the rate of change is practically independent of initial concentration and pH. Results

such as those of Fig. 4 were obtained by starting with unreduced quinone in the polarographic cell, and, with nitrogen bubbling through the solution to promote rapid mixing, adding the calculated equivalent amount of standard dithionite from a microburette as rapidly as possible. Nitrogen-bubbling was continued for 1 minute after the addition, and then periodically the current was measured at a potential of −0·45 v (S.C.E.), corresponding to the bottom plateau of the anthraquinol anodic wave; time was measured with a stop-watch from the point when half the dithionite had been added.

Table 3 gives the variation with time of the relative height of the anodic wave

TABLE 3. *Effect of temperature on time-dependence of wave-height for* 10^{-3}M-*hydroxyanthraquinone, fully reduced, in aqueous buffer,* pH 9·40, *ionic strength* 0·1.

t (min. after adding $Na_2S_2O_4$)		0	1·5	3	4·5	6	9	12
Relative wave height	15°	100	89·0	79·6	70·4	63·3	51·5	45·5
	25°	100	82·2	65·8	57·5	47·6	34·3	29·8
	35°	100	70·5	54·4	39·9	30·1	21·6	17·3
t (min. after adding $Na_2S_4O_3$)		15	20	25	30	35	40	∞ (extrap.)
Relative wave height	15°	39·6	33·6	27·7	24·8	22·8	21·2	20·0
	25°	24·3	21·9	21·0	19·7	18·9	18·6	18·6
	35°	15·3	13·8	13·2	12·9	12·9	12·9	12·9

of 2-hydroxyanthraquinol at three different temperatures, pH and ionic strength being kept constant. Clearly, the rate of change and also the final equilibrium extent of the change increase with rise of temperature.

DISCUSSION

Identification of Conversion Product.—The complete regeneration of 2-hydroxyanthraquinone on reoxidation strongly suggests that the conversion product of the quinol is the corresponding oxanthranol, by analogy with the systems (I) ⇌ (II) and (III) ⇌ (IV). This view is supported by the fact that the product from 2-hydroxyanthraquinol gives a reduction wave with E_m about −1·2 v (S.C.E.) (Figs. 1 and 3), whereas Stone and Furman (*J. Amer. Chem. Soc.*, 1948, **70**, 3062) find that 10-hydroxy-10-methylanthrone (V), *i.e.*, 10-methyloxanthranol, gives in 40% dioxan at 25° at apparent pH 7—10 a two-electron reduction wave with similar diffusion current constant and E_m about −1·3 v (S.C.E.) in phosphate or borate buffers, which value they state is not likely to be greatly different in aqueous solutions. The conversion product of 2 : 6-dihydroxyanthraquinol gives a similar wave (Fig. 2) with E_m about −1·55 v (S.C.E.). The shift in E_m here due to the second substituent hydroxy-group (−0·35 v) is similar in direction to but greater than the corresponding effect (−0·14 v) in the anthraquinones (preceding paper).

For all three substituted oxanthranols, the height of the reduction wave corresponds to a two-electron process, the product of which is probably the corresponding anthrone. Supporting evidence is given by the appearance of a wave at about −1·35 v (S.C.E.), merging with the top of the 2-hydroxyoxanthranol wave, in Fig. 1. This wave would be expected for 2-hydroxyanthrone by comparison with the wave given by unsubstituted anthrone at about −1·0 v (S.C.E.) in alkaline buffers in 40% dioxan (Stone and Furman, *loc. cit.*), and at about −1·27 v in 50% ethanol (Day and Kirkland, *ibid.*, 1950, **72**, 2766), if we assume that the effect of the 2-hydroxy-group on the E_m of anthrone is similar to that of the 6-hydroxy-group on the E_m of 2-hydroxyoxanthranol.

Identification of Tautomerising Species.—Since the equilibrium fractional conversion into tautomer is independent of initial concentration of 2-hydroxyanthraquinol and of pH (Fig. 4), the tautomerisation may be represented by X ⇌ Y, where X represents the anthraquinol in an un-ionised or incompletely ionised state (since on complete ionisation at pH ≈13 it no longer tautomerises), and Y represents the tautomer, 2-hydroxyoxanthranol, in a corresponding state of ionisation. Lower-case italic letters being used to denote concentrations of species represented by the corresponding capital letters, the tautomerisation equilibrium constant is

$$K' = y/x = (y/r)(r/x)$$

where r is the total concentration of the anthraquinol (R) in all four states of ionisation

A, B, C, D, corresponding to ionisation of 0, 1, 2, and 3 hydroxy-groups, respectively. It is shown in Appendix I that, at any fixed pH, the ratios a/r, b/r, c/r, and d/r are independent of r. Since X is one or other of A, B, and C, r/x is also independent of r, and thus K' is proportional to y/r, for a given pH.

The value of y cannot be obtained from the height of the oxanthranol reduction wave, since this is ill-defined (Fig. 1). It is given, however, by the equilibrium decrease in height of the original wave at about −0·7 v (S.C.E.). In the same arbitrary units, the value of r is obtainable from the height of this same wave as follows. The wave height is equal to $r + s + t$, where s and t denote the concentrations of anthra-semiquinone and anthraquinone species in the solution. Geake (*Trans. Faraday Soc.*, 1938, **34**, 1395) has shown that

$$t/s = 1\sqrt{PK};\ r/s = \sqrt{P/K}, \text{ where } P = e^{2F(E^{\circ\prime} - E)/RT}$$

and K is the semiquinone formation constant; $E^{\circ\prime}$, the virtual standard redox potential for a given pH, may be replaced by E_m, and E, the potential of an inert electrode, may be replaced by the potential of the dropping mercury electrode at the point on the wave where the current is zero, since then the composition of the solution at the mercury-drop interface is identical with that of the bulk of the solution.

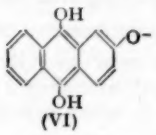
Applying these equations to the results in columns 2—4 of Table 2, with the value of K obtained from the preceding paper, we obtain the figures in the last six columns of the table. The variability of y/s indicates that the semiquinone is not the tautomerising species, and since the quinone does not tautomerise, the quinol must be the form which does tautomerise. This is confirmed by the approximate constancy of y/r. A similar constancy is found at other pH values, but the value of this ratio varies with pH as shown in Table 4, having a maximum at a pH between 8·85 and 9·59. In Appendix II it is shown that a/r increases to an asymptotic maximum as pH increases, d/r behaves similarly as pH decreases, c/r is maximal at pH ~11·32, and b/r maximal at pH ~9·38. Hence X may be identified with B (VI).

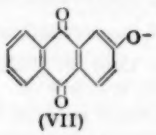
TABLE 4. *Equilibrium* y/r *values at* 25° : *variation with* pH.

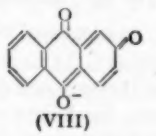
pH	13·79	12·87	12·00	11·27	9·59	9·40	8·85	6·0 *
y/r	0·00	0·03	0·13	1·7	4·1	4·4	4·2	0·00

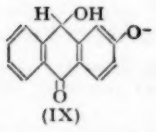
* 50% Ethanol required to dissolve quinone.

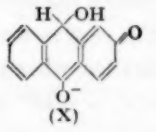
Explanation of the Tautomerism.—Unreduced 2-hydroxyanthraquinone, in the ionised state corresponding to that of the tautomerising form B of the quinol, is stabilised by ionic *para*-resonance of the type (VII) ⟷ (VIII), which is estimated to shift the redox potential by −120 mv (preceding paper), equivalent to increase in stabilisation of the quinone relatively to the quinol by about 5·5 kcal. per g.-mol. Upon reduction to the

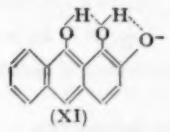

(VI)


(VII)


(VIII)


(IX)


(X)


(XI)

quinol, this resonance possibility is lost, but may be regained by tautomerisation to (IX) ⟷ (X). Since at least one hydroxy-group in 2-anthraquinol must be ionised to permit *para*-resonance, while at least two hydroxy-groups must be un-ionised to permit tautomerism, only the species B can fulfil these conditions, confirming the conclusion already reached. A similar explanation applies to 2 : 6-dihydroxyanthraquinol. The anomalous absence of tautomerism in 1 : 2-dihydroxyanthraquinol, in spite of the presence of a 2-hydroxy-

group, is probably the result of stabilisation of the quinol by hydrogen bonding involving the 1-hydroxy-group, as in (XI), and also a steric hindrance effect of this group in the oxanthranol.

Branch and Calvin ("The Theory of Organic Chemistry," Prentice-Hall Inc., 1941, p. 291) have shown that ΔH for the change anthranol $\longrightarrow$ anthrone is very small. If we make the reasonable assumption that, for the related change anthraquinol $\longrightarrow$ oxanthranol, ΔH and thus the resonance energy stabilising oxanthranol relatively to anthraquinol are very small, we may calculate approximately the tautomerisation equilibrium constant K'' for the latter change, as follows. Combining the values of y/r for 2-hydroxyanthraquinol at pH 8·85 and 9·59 (Table 4) with the corresponding values of b/r calculated from the information given in Appendix I, the mean value obtained for the tautomerisation equilibrium constant $K' = y/b$ for the species B is about 8·2. The resonance energy stabilising the oxanthranol in this case is about 5·5 kcal., and thus the difference in resonance energy for the two systems is also about 5·5 kcal. Hence

$$5500 = \boldsymbol{R}T \ln K'/K'' = 596 \ln 8{\cdot}2/K''$$

whence $K'' = 0{\cdot}001$ approx. This is in keeping with the observation that in alcoholic hydrochloric acid anthraquinol is only 3% converted into oxanthranol at equilibrium

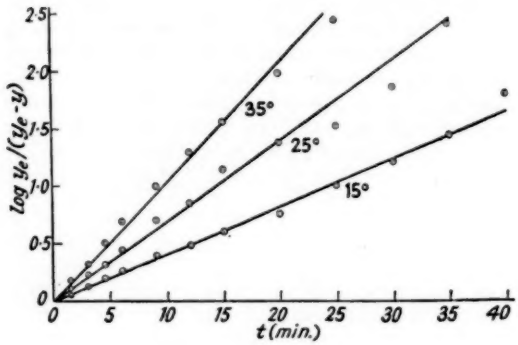


FIG. 5. 10^{-2}M-2-*Hydroxyanthraquinol*: pH 9·40; $I = 0{\cdot}1$.

Verification of first-order kinetics of tautomerisation.

(Karrer, "Organic Chemistry," Elsevier, 1947, p. 578). A similar result may be expected for all the anthraquinols studied in the preceding paper, other than the 2-hydroxy- and the 2 : 6-dihydroxy-derivative. This would explain why these other compounds gave no polarographic indication of tautomerisation.

Kinetics of the Tautomerisation of 2-Hydroxyanthraquinol.—Assuming that the reaction is $B \underset{k'}{\overset{k}{\rightleftharpoons}} Y$, as suggested by the rate of the forward reaction being independent of r or pH, we have $dy/dt = kb - k'y$. For the data of Table 3, which refer to fully reduced 2-hydroxyanthraquinone at a fixed pH, $b = k''r$ (k'' is a constant), and since s and t are virtually zero, the height of the main wave is equal to $r = r_0 - y$, where r_0 is the initial value of r, before appreciable tautomerisation has occurred. Thus

$$dy/dt = kk''r - k'y = kk''(r_0 - y) - k'y = kk''r_0 - y(kk'' + k')$$

At the completion of tautomeric equilibration, when $y = y_e$ and $dy/dt = 0$,

$$0 = kk''r_0 - y_e(kk'' + k')$$

and thus by subtraction

$$dy/dt = (y_e - y)(kk'' + k')$$

which upon integration and insertion of the condition $y = 0$ at $t = 0$ gives

$$\log y_e/(y_e - y) = t(kk'' + k')/2{\cdot}303$$

The data of Table 3 lead to plots of $\log y_e/(y_e - y)$ against t which, at least for the earlier t values, where sensitivity to error in the extrapolated y_e value is small, are linear and pass

through the origin (Fig. 5), confirming the last equation and the assumption of first-order kinetics for both directions of the tautomerisation reaction.

From the same data for $t \leqslant 9$ minutes, where y is small and the reverse reaction velocity is negligible, values of kk'' for three temperatures were obtained from the slopes of plots of $\log r$ against t, which are linear. The slope of the linear plot of $\log kk''$ against $1/T$ gave the apparent activation energy of the reaction $R \longrightarrow Y + H^+$ as 8·67 kcal./mol. This is the sum of the activation energy of the tautomerisation $B \longrightarrow Y$ and the unknown heat of the ionisation $R \longrightarrow B + H^+$.

Appendix I.

$$A = B + H^+;\ bh/a = K_1^r;\ b = K_1^r a/h$$
$$B = C + H^+;\ ch/b = K_2^r;\ c = K_2^r b/h = K_1^r K_2^r a/h^2$$
$$C = D + H^+;\ dh/c = K_3^r;\ d = K_3^r c/h = K_1^r K_2^r K_3^r a/h^3$$

For 2-hydroxyanthraquinol, $pK_1^r = 8{\cdot}70$, $pK_2^r = 10{\cdot}05$, $pK_3^r = 12{\cdot}60$ (preceding paper). Also

$$r = a + b + c + d = a(1 + K_1^r/h + K_1^r K_2^r/h^2 + K_1^r K_2^r K_3^r/h^3)$$
$$= a(h^3 + K_1^r h^2 + K_1^r K_2^r h + K_1^r K_2^r K_3^r)/h^3 = af/h^3$$

where f = the factor in parentheses. Thus $a/r = h^3/f$, $b/r = K_1^r h^2/f$, $c/r = K_1^r K_2^r h/f$, and $d/r = K_1^r K_2^r K_3^r/f$. These four fractions are functions of h (pH) but are independent of r.

Appendix II.

From Appendix I, $a = h^3 r/f$, and hence at constant r,

$$\partial a/\partial h = [3rh^2 f - h^3 r(3h^2 + 2K_1^r h + K_1^r K_2^r)]/f^2 = h^2 r(2K_1^r K_2^r h + 3K_1^r K_2^r K_3^r + K_1^r h^2)/f^2$$

This is always positive, hence a increases as h increases, until, when $h > K_1^r > K_2^r > K_3^r$, $\partial a/\partial h \to 0$ and $a \to r$, as is obvious from first principles.

Similarly, $b = K_1^r rh^2/f$, and thus at constant r,

$$\partial b/\partial h = K_1^r rh(K_1^r K_2^r h + 2K_1^r K_2^r K_3^r - h^3)/f^2$$

This equals zero when $h^3 = K_1^r K_2^r(h + 2K_3^r) \approx K_1^r K_2^r h$ if we assume that $h \gg K_3^r$. Thus b is maximal when $h = (K_1^r K_2^r)^{\frac{1}{2}}$, or $pH = \frac{1}{2}(pK_1^r + pK_2^r) = \frac{1}{2}(8{\cdot}70 + 10{\cdot}05) = 9{\cdot}38$.

The assumption that $h \gg K_3^r$ is thus justified, since $pK_3^r = 12{\cdot}60$. That b is maximal and not minimal is shown by the negative value of $\partial^2 b/\partial h^2$ when $h = (K_1^r K_2^r)^{\frac{1}{2}}$.

Since $c = K_1^r K_2^r hr/f$, we have at constant r, $\partial c/\partial h = K_1^r K_2^r r(K_1^r K_2^r K_3^r - K_1^r h^2 - 2h^3)/f^2$, which equals zero when $0 = 1 - h^2/K_2^r K_3^r - 2h^3/K_1^r K_2^r K_3^r \approx 1 - h^2/K_2^r K_3^r$ if we assume that $K_1^r \gg h$. This gives $h = (K_2^r K_3^r)^{\frac{1}{2}}$, or $pH = \frac{1}{2}(pK_2^r + pK_3^r) = \frac{1}{2}(10{\cdot}05 + 12{\cdot}60) = 11{\cdot}32$. Since $pK_1^r = 8{\cdot}70$, the assumption $K_1^r \gg h$ is justified. The value $h = 11{\cdot}32$ makes $\partial^2 c/\partial h^2$ negative, and thus corresponds to a maximum for c.

Since $d = K_1^r K_2^r K_3^r r/f$, we have at constant r, $\partial d/\partial h = -K_1^r K_2^r K_3^r r(3h^2 + 2K_1^r h + K_1^r K_2^r)/f^2$, which is always negative. Thus d decreases as h increases, tending to zero when $h \gg K_1^r > K_2^r > K_3^r$, as is obvious from first principles.

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Technical College, Bradford, Yorks.
Medway Technical College, Gillingham, Kent. [*Received, December 13th*, 1951.]

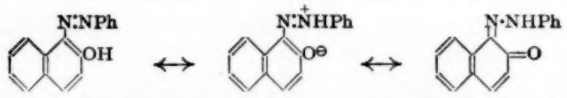
342. *Researches on Monolayers. Part II.* The Effect of Acid and Alkali upon Monolayers of Aromatic Azo-compounds containing Long Alkyl Chains.*

By C. H. Giles and E. L. Neustädter.

The apparent molecular areas and compressibilities of aromatic hydroxyazo-compounds containing long alkyl chains have been measured in monolayers on dilute acid and alkali. In accordance with published data, the *p*-hydroxy-compounds appear to exist almost completely in the azo-form. The *o*-compounds appear to contain much of the hydrazone form, but the results do not give decisive evidence of the presence or absence of the azo-tautomer in this series, except in one case, where an *oo'*-dihydroxyazo-compound appears to contain the azo-form.

The determination of molecular areas and orientation of aromatic hydroxyazo-compounds containing long alkyl (C_{12}—C_{18}) chains, in monolayers on water, has been described in Part I.* The work has now been extended by a study of the influence of acid or alkali upon the films, in order to determine whether by this means the presence of a chelate link in *o*-hydroxyazo-compounds or of the quinone hydrazone tautomer in either type of azo-compound could be detected.

The Structure of Hydroxyazo-compounds.—It is well known that many aromatic hydroxyazo-compounds appear to co-exist with the corresponding quinone hydrazone tautomers, but the evidence for the exact formulation of the *o*- and *p*-series is somewhat conflicting (see Sidgwick's "The Organic Chemistry of Nitrogen," Taylor and Baker, Clarendon Press, Chap. XIV). Some authors have claimed that *o*-hydroxyazo-compounds exist only in the quinonoid form, and some state that *p*-compounds are preponderantly in the azo-form. It has also been suggested that resonance of both forms with a third zwitterion configuration may occur in the *o*-hydroxyazo-series (Kuhn, *Naturwiss.*, 1932, **20**, 618), whereby the forms of phenylazo-β-naphthol can be represented thus :



Burawoy and Markowitsch-Burawoy (*J.*, 1936, 36), however, following studies of absorption spectra, stated that the similarity between 2-phenylazo-1-naphthol and its *N*-phenyl derivative, and the difference between these two on the one hand and the corresponding *O*-methyl ether on the other, exclude the interpretation of the structure of the *o*-hydroxyazo-compounds as resonance hybrids.

Chelation of the hydroxy-group with the adjacent azo-group has been detected in water-insoluble *o*-hydroxyazo-compounds when dissolved in organic solvents (Mason, *J. Soc. Dyers Col.*, 1932, **48**, 293; Hendricks, Wulf, Hilbert, and Liddell, *J. Amer. Chem. Soc.*, 1936, **58**, 1991). This fact has usually been considered to account for the insolubility of such compounds in aqueous alkali, but Burawoy (Discussion on paper by Desai and Giles, *J. Soc. Dyers Col.*, 1949, **65**, 639) has pointed out that *o*-nitrophenol, which contains a chelate bond, is nevertheless a stronger acid than the *m*- and the *p*-isomer, and therefore he considers that the insolubility of *o*-hydroxyazo-compounds in alkali is not due to such a bond, but rather to their existence entirely as quinone hydrazones.

Effects of Ionisation in Monolayers.—Ionisation of water-attracting groups in a monolayer, on water, by addition of acid or alkali, as appropriate, *e.g.*, the addition of alkali to the water below a monolayer of a phenol, or of an acid to the water below a monolayer of a base, increases the apparent molecular area of the monolayer compound owing to the mutual electrostatic repulsion of the ions (Adam, "The Physics and Chemistry of Surfaces," Oxford Univ. Press, 3rd edn., 1941, Chap. II). Adam and Miller (*Proc. Roy. Soc.*, 1933,

* Part I, *J.*, 1952, 918.

A, **142**, 401), for example, found that the molecular areas of long alkyl-chain phenols increased when 2N-sodium carbonate or 2N-sodium hydroxide solutions were used as substrates, for, whereas all the phenols tended to give a molecular area of 24 Å² on water,

FIG. 1. *Areas on* 0·1N-HCl (*abscissæ*).

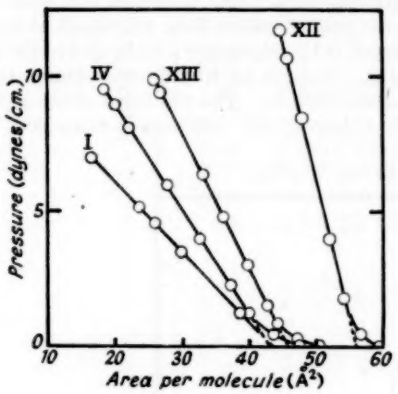


FIG. 2. *Areas on* 0·1N-HCl (*abscissæ*).

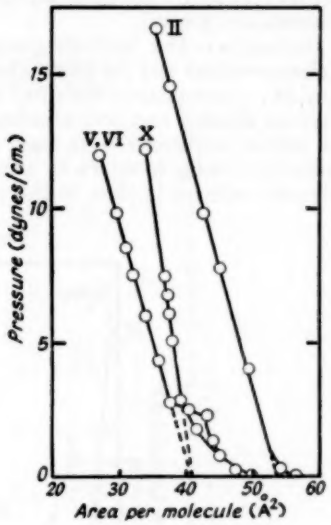


FIG. 3. *Areas on* 0·1N-HCl.

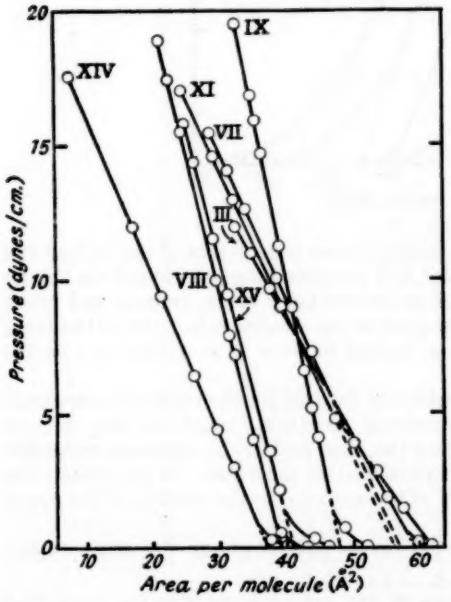
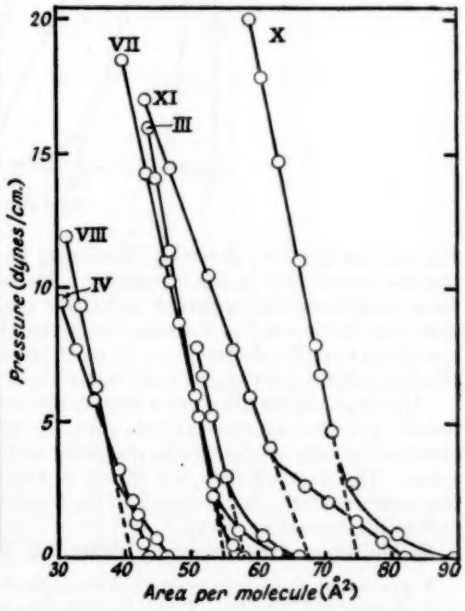


FIG. 4. *Areas on* 0·1N-Na_2CO_3.



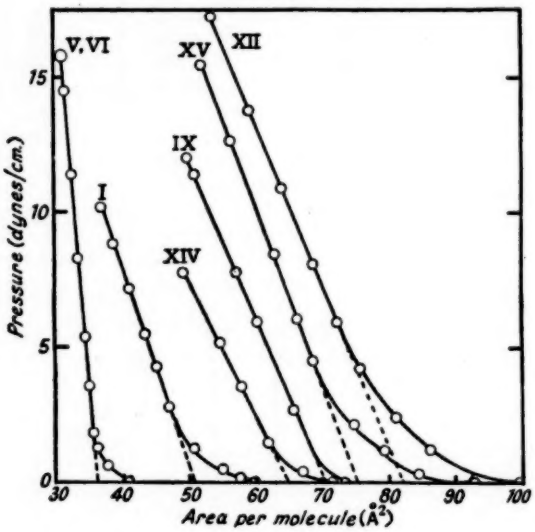
those of *p*-dodecyl- and *p*-hexadecyl-phenol increased to *ca.* 42·5 Å² and *ca.* 28·5 Å², respectively, on 2N-sodium carbonate solution at 16°. When Adam and Miller's curves are replotted to the scales used in the figures of the present paper, the increases in

compressibility are *ca.* 0·06 and 0·01, respectively, and these may be attributed to the greater intermolecular distances in the expanded films.

It was thought that an investigation of the behaviour, as monolayers on aqueous acid and alkaline solutions, of the surface-active hydroxyazo-compounds already described by us (Part I, *loc. cit.*) might provide new evidence relating to the configuration of hydroxyazo-compounds in general.

Discussion.—The hydroxy-group of the azo-form would be expected to ionise on alkaline solutions and the imino-group of the quinone form might ionise on acid solutions. Many of the compounds described in Part I have now therefore been examined as monolayers on alkaline and acid solutions. Unbuffered 0·1N-solutions *† of hydrochloric acid and sodium carbonate were used as substrates. Sodium hydroxide was found to be unsuitable ‡ owing to attack by atmospheric carbon dioxide. The pH value of the sodium carbonate solution is close to the probable pK values of the compounds examined, and

FIG. 5. *Areas on* 0·1N-Na_2CO_3.



hence if the azo-form is present there may be roughly equal proportions of the ionised and the un-ionised form in the monolayer. Marsden and Schulman (*loc. cit.*) found that under these conditions the apparent molecular areas of certain fatty acids, amines, and esters were at a minimum and increased on either the acid or the alkaline side. As will be seen, the present results demonstrate in most cases a decided increase in molecular area on the alkaline solution, compared with water alone.

Although the results show a reasonable consistency throughout the series of compounds tested, yet the interpretations must be considered tentative, based as they are on observation only of changes in compressibility of the films and in the apparent molecular areas. The detailed data are shown in the figures and in the table; in the latter, the film compressibility is expressed by the tangent of the angle (α) to the vertical of the upper part of the force–area curve.

If ionisation takes place at either an $-OH$ or a $>NH$ group we may expect

* For one compound (X) the data in the Table refer to 1·0N-solutions.

† Marsden and Schulman (*Trans. Faraday Soc.*, 1938, **34**, 748) and Adam and Miller (*loc. cit.*) noticed certain anomalous effects due to the salts present when buffers were used as substrates.

‡ Adam and Miller (*loc. cit.*) found that some films tended to collapse on 0·1N-sodium hydroxide, perhaps because of excessive solubility of the monolayer molecules. In the present experiments (II) was found to have an area of *ca.* 150 Å² on 0·1N-sodium hydroxide.

Effect of acid and alkali on compressibilities and apparent molecular areas of hydroxyazo-compounds in monolayers.

No.	Compound: Diazo-component	Compound: Coupling component	θ ¶	Apparent molecular area at zero compression (Å²) and compressibility (tan α) § on: Water Å²	Water tan α	0·1N-HCl Å²	0·1N-HCl tan α	0·1N-Na_2CO_3 Å²	0·1N-Na_2CO_3 tan α	ΔÅ² (%) and Δ tan α: 0·1N-HCl ΔÅ² (%)	0·1N-HCl Δ tan α	0·1N-Na_2CO_3 ΔÅ² (%)	0·1N-Na_2CO_3 Δ tan α
	o-Hydroxyazo-compounds.												
I	*p*-NHPh·$C_{12}H_{25}$	*p*-C_6H_4Me·OH	45°	44·5	0·11	44	0·97	51	0·33	0	0·86	15	0·22
II	,,	β-$C_{10}H_7$·OH	60	42·5	0·16	53	0·25	58	0·21	24	0·09	36	0·05
III	,,	3-$C_{14}H_9$·OH †	65	50	0·23	59	0·53	55	0·18	18	0·30	10	−0·05
IV	*p*-NHPh·$C_{16}H_{33}$	β-$C_{10}H_7$·OH	60	44·5	0·05	43	0·65	44	0·33	−4	0·60	−1	0·28
V	NH_2Ph	*p*-$C_{16}H_{33}$·C_6H_4·OH	90	32	0·07	40	0·27	36	0·09	25	0·20	12	0·02
VI	,,	*p*-$C_{16}H_{37}$·C_6H_4·OH	90	32	0·07	40	0·27	36	0·09	25	0·20	12	0·02
VII	*m*-NH_2·C_6H_4·$CO_2C_{16}H_{33}$	β-$C_{10}H_7$·OH	55	57	0·28	57	0·43	56	0·21	0	0·15	−2	−0·07
VIII	*p*-NH_2·C_6H_4·O·$C_{16}H_{33}$	,,	55	38	0·05	39	0·21	41	0·19	2·5	0·16	8	0·14
	oo'-Dihydroxyazo-compound.												
IX	*o*-NH_2·C_6H_4·OH	*p*-$C_{16}H_{33}$·C_6H_4·OH	80	47	0·09	47	0·19	70	0·43	0	0·10	49	0·34
	p-Hydroxyazo-compounds.												
X	*p*-NHPh·$C_{12}H_{25}$ *	1-$C_{14}H_9$·OH ‡	90(?)	41	0·07	40	0·11	75	0·18	−3	0·04	83	0·11
XI	*m*-NH_2·C_6H_4·$CO_2C_{16}H_{33}$	*o*-C_6H_4Me·OH	60	53	0·25	56	0·45	68	0·33	6	0·20	28	0·08
XII	,,	α-$C_{10}H_7$·OH	60	55	0·36	56	0·23	82	0·40	2	−0·13	49	0·04
XIII	*p*-NH_2·C_6H_4·$CO_2C_{16}H_{33}$	*o*-C_6H_4Me·OH	50	44	0·09	46	0·51	—	—	5	0·42	—	—
XIV	*p*-NH_2·C_6H_4·O·$C_{16}H_{33}$	,,	90(?)	36	0·07	37	0·40	65	0·49	2·5	0·33	80	0·42
XV	,,	α-$C_{10}H_7$·OH	90(?)	38	0·18	41	0·25	75	0·36	8	0·07	97	0·18

* The data for this compound were obtained on 1N-solutions of HCl and Na_2CO_3.
† 3-Hydroxyphenanthrene.
‡ 1-Hydroxyanthracene.
§ Where α is the deviation from the vertical of the upper portion of the *F–A* curves in Figs. 1—5.
¶ Where θ is the probable orientation angle on water alone (see Part I).

some or all of the following changes to occur in the monolayer: (*a*) Mutual repulsion of the surface-active ions in the monolayer, leading to an increase in both apparent molecular area and compressibility. (*b*) A change in the balance of forces determining the orientation of the monolayer molecules relatively to the water surface, caused by changes in solubility of the ionisable groups. Thus the –OH group should be reduced in solubility by acid and increased by alkali, and the >NH group should behave in the reverse manner. The molecular orientation might then change, and either a decrease or an increase in molecular cross-section at the water surface would take place, depending, *e.g.*, upon the bulkiness of the under-water " head " group and the orientation of the several substituent groups. Such a change might mask, or be masked by, film expansion due to ionic repulsion, but if so, the latter would still be made evident by an increase in compressibility. (*c*) Partial collapse of the shorter (C_{12}) alkyl chain present in many of the compounds used, if ionic repulsion forces the molecules apart. Its length is so near the minimum required to form solid films that if the " head " groups are mutually repelled the chains may have insufficient cohesion to prevent partial collapse into intermolecular gaps, towards the water surface. If this occurred, the result might be an increase in film area without increase in compressibility. (*d*) In addition, the presence of alkaline solution may cause some degree of hydrolysis of the ester groups in (VII), (XI), (XII), and (XIII). This would lead to a decrease in film area without change in compressibility, because the azo-molecule would be replaced by a long-chain alcohol with a smaller " head " group. The following more detailed discussion of the results shows that most of them can be explained on the basis of one or more of these four effects.

o-*Hydroxyazo-compounds.—On acid.* Compounds (I), (IV), (VII), and (VIII) show little or no increase in molecular area but large increases in compressibility. There is probably ionisation and re-orientation of the molecule. Compound (I), in particular, which has only a benzene ring " head " group and has a very low orentation angle on water, is now able to occupy much less space at the surface because the reduced solubility of the hydroxy-group enables the orientation angle to approach much nearer to 90°. The smallness of the compressibility change of (II) may be due to partial collapse of the alkyl chain as discussed at (*c*) above; (III) has a much larger compressibility increase than (II), perhaps because the larger and more unsymmetrical shape of the under-water " head " leaves greater intermolecular gaps at the surface.

Compounds (V) and (VI) are believed to stand nearly vertically on water and should not therefore change their orientation. They also have C_{16} chains, which would not be expected to collapse, so that the observed increase in area and compressibility must be due largely to ionisation.

On alkali. The area increases of this series, coupled with their mostly rather small increases in compression, could be accounted for by re-orientation due to decreased solubility of an >NH group in the hydrazone tautomer and they are therefore not certain evidence of the presence of an azo-form. The increase of compressibility of (I) would then be due to the greater mobility of the small " head " group, and that of (VIII) to re-orientation caused by the solubility of the ether group increasing relatively to that of the >NH group. Hydrolysis of the ester group in (VII) can account for the decreases in area and compressibility.

The evidence, however, is not decisive enough to exclude the possibility that the hydroxyazo-form is present in this series. If it is present, then the effect of alkali is evidence of an increased solubility of the hydroxy-group, which in that case is not chelated with the adjacent azo-group. In the monolayer, each molecule is in direct contact with water and thus if any azo-tautomer is present, the hydroxy-group may be prevented from bonding with the proximate azo-group by preferential linkages with water.

Compound (IV), which differs from (II) only in having a longer alkyl chain, shows an increase in compressibility but a slight decrease in area. The differences could be explained by a re-orientation of the molecule of (IV) masking the intermolecular repulsion caused by ionisation of the hydroxy-group and a partial collapse of the alkyl chain in (II) interfering with such a change.

The difference here evident in the behaviour of (II) and (IV) is therefore more easily

explained by assuming that a hydroxy-form is present, so that on the whole it is not possible to state that *no* hydroxy-form is present in the *o*-hydroxyazo-series.

oo'-Dihydroxyazo-compound (IX).—This shows considerable increase in area and compressibility on alkali, evidently due to ionisation, and rather smaller changes on acid. (Even if this compound were wholly in the quinone hydrazone form, one free hydroxy-group would remain).

A study of the structure of (IX) and its orientation at the surface shows that the hydroxy-groups are symmetrically placed in a horizontal line on either side of the azo-group. If, therefore, the compound were *wholly* in the azo-form, the effect of the acid substrate in reducing the solubility of the hydroxy-groups relative to that of the azo-group should cause no change in orientation or in area. The observed changes must therefore be evidence that the compound is *not* wholly an azo-structure.

p-*Hydroxyazo-compounds.—On acid.* These compounds display very small area increases [(X) in fact decreases] and with the exception of the *o*-cresol compounds (XI, XIII, XIV), where re-orientation would be most expected, no appreciable increase in compressibility occurs. It would appear therefore that very little of the quinone hydrazone tautomer is present in this series of compounds.

On alkali. All the compounds examined increase considerably in area, especially (XIV) and (XV), which also increase appreciably in compressibility. The small compressibility change of (XI) and (XII) and their lower degree of expansion are probably due to partial hydrolysis. Compound (X) has a very large and unwieldy under-water "head" and re-orientation of this may account for the smaller change in compressibility compared with (XIV) and (XV), though it has been found difficult to demonstrate the effect on models.

The behaviour of the two *p*-dodecylaniline → cresol compounds may be additional evidence for the preponderance of the hydrazone form in the *o*-hydroxyazo-series. *p*-Dodecylaniline → *o*-cresol, which has the hydroxy-group *p*- to the azo-group, is too soluble to form a film (see Part I). The film-forming properties of the *o*-hydroxy-isomer (from *p*-cresol), however, might be attributed to the absence of a hydroxy-group and the consequent reduced water-solubility, or the reduced solubility might be due to chelation of the azo- and the hydroxy-group.

Conclusion.—The general conclusion is that the water-insoluble *p*-hydroxyazo-compounds appear to exist almost completely in the azo-form, whereas the corresponding *o*-hydroxyazo-compounds contain the hydrazone form. The evidence for the presence of the azo-form in the latter series is equivocal (except possibly in the case of the *oo'*-dihydroxyazo-compound, where the evidence appears to be positive). This is in general agreement with much of the published information.

Experimental.—The film balance, the general technique used, and the preparation of the azo-compounds (except IX) have been described in Part I. In place of distilled water alone, solutions of hydrochloric acid (0·1N) and sodium carbonate (0·1N) both of analytical reagent quality, in distilled water, were employed as substrates. The molecular area figures are each the mean of at least four successive determinations repeated on fresh films, and were found to be reproducible to ± 1 Å^2. The conclusions have been checked by the use of scale-model molecules.

o-*Aminophenyl* → p-*hexadecylphenol* (IX). *o*-Aminophenol (5·5 g.) was diazotised by Reisenegger's method (*Annalen*, 1884, **221**, 314) and coupled with *p*-hexadecylphenol (16 g.) in aqueous sodium hydroxide; red prisms (from glacial acetic acid and ethanol successively), m. p. 84—85° (Found: C, 76·5; H, 9·3; N, 6·2. $C_{28}H_{42}O_2N_2$ requires C, 76·7; H, 9·6; N, 6·4%).

1-*Hydroxyanthracene.* This compound (α-anthranol), used in the work reported in Part I, was prepared by alkali fusion of the sodium salt of the sulphonic acid.

We thank Professor P. D. Ritchie for his interest and encouragement and the Directors of Imperial Chemical Industries Ltd., Dyestuffs Division, for financial assistance to one of us (E. L. N.) and for the gift of intermediates.

DEPARTMENT OF TECHNICAL CHEMISTRY,
ROYAL TECHNICAL COLLEGE, GLASGOW, C.1.

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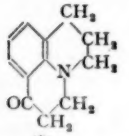
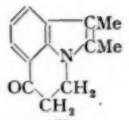
343. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part V.* Derivatives of* 1 : 2-*Dihydro*-1-*keto*-4 : 5-*dimethyl-liline.*†

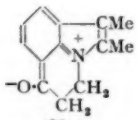
By C. Y. Almond and Frederick G. Mann.

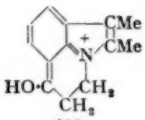
1-2′-Carboxyethyl-2 : 3-dimethylindole on cyclisation furnishes 1 : 2-dihydro-1-keto-4 : 5-dimethyl-liline. The properties of this compound have been investigated for comparison with those of other cyclic keto-amines, and particularly with those of the structurally analogous 1-ketojulolidine. The keto-liline gives a phenylhydrazone which furnishes a ψ-indole. The keto-liline, when subjected to the Pfitzinger reaction with isatin followed by decarboxylation, gives a quinolinoliline which, unlike the corresponding juloline derivative, does not show isomeric forms but resembles this derivative in undergoing ready oxidation to a cyclic amide.

Previous papers in this series (*J.*, 1949, 2816; 1951, 1898, 1906, 1909) have recorded investigations on the structure and properties of the indolo- and quinolino-derivatives obtained from various cyclic keto-amines and keto-sulphides by the Fischer indolisation and the Pfitzinger reactions respectively. In particular, it was shown by Mann and Smith (*J.*, 1951, 1898) that 1-ketojulolidine (I) (*a*) when converted into its phenylhydrazone and then indolised gives a ψ-indole, and (*b*) when subjected to the Pfitzinger reaction and then decarboxylated gives a quinolino-derivative which exists in two distinct and inter-


(I)


(II)


(IIa)

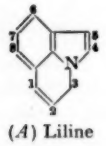

(III)

convertible isomeric forms, both of which, however, undergo very ready atmospheric oxidation to the same cyclic amido-derivative. Although the formation of a ψ-indole, and the ready oxidation of the quinolino-base, had been encountered with other similar polycyclic systems, the occurrence of isomerism in the quinolino-base and its derivatives was novel, and we have therefore investigated the properties of the corresponding derivatives obtained from 1 : 2-dihydro-1-keto-4 : 5-dimethyl-liline (II), in which the ring system differs from that of (I) only by the replacement of the hydrogenated pyridine ring by a pyrrole ring.

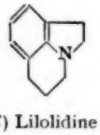
2 : 3-Dimethylindole, when heated with vinyl cyanide in the presence of sodium methoxide (B.P. 457,621), is readily converted into 1-2′-cyanoethyl-2 : 3-dimethylindole, but attempts to cyclise this nitrile directly to 1 : 2-dihydro-1-keto-4 : 5-dimethyl-liline by the action of aluminium chloride under various conditions [cf. F.P. 806,715; F.I.A.T. Final Report No. 1298 (1949); Mann and Smith, *loc. cit.*] gave unsatisfactory results. The

* Part IV, *J.*, 1951, 1909.

† *Note on Nomenclature.* Bamberger and Sternitzki (*Ber.*, 1893, **26**, 1298) gave the names liloline and lilolidine to the compounds (*B*) and (*C*) respectively. We have therefore termed the compound


(*A*) Liline

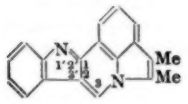
(*B*) Liloline


(*C*) Lilolidine

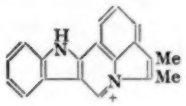
(*D*) Juline

(*A*) liline, and the names of the three compounds thus form a series corresponding to juline (*D*), juloline, and julolidine (cf. Mann and Smith, *J.*, 1951, 1898): the liline ring system is numbered as in (*A*) to correspond to that of juline (*D*).

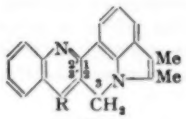
nitrile was therefore hydrolysed to 1-2′-carboxyethyl-2 : 3-dimethylindole, which with phosphoric anhydride in boiling xylene readily gave 1 : 2-dihydro-1-keto-4 : 5-dimethylliline (II). There is little doubt that this exists as a resonance hybrid to which the covalent form (II) and the polar form (II*a*) contribute, and moreover that the relative contribution of each form depends on the chemical environment. It is noteworthy that the crystalline keto-amine is yellow, but that its solution in concentrated hydrochloric acid is red, in acetic acid yellow, and in carbon tetrachloride very pale yellow (almost colourless). Since the ionic quinonoid form (II*a*) would undoubtedly be more intensely coloured than the covalent form (II), these results indicate that the proportion of the polar form is greatest in strongly acid media : moreover, it is probable therefore that it is the polar form which unites with acids to give the cation (III). Even so, these salts apparently exist only in strongly acid solution, and are too unstable to exist in the solid state. In these properties the keto-amine (II) strongly resembles both the 1-ketojulolidine and also 1 : 2 : 2*a* : 3 : 4 : 5 : 8 : 9 : 10 : 10*a*-decahydro-5 : 8 -diketo-2*a* : 10*a*-diazapyrene (Almond and Mann, *J.*, 1951, 1906).



(IV)



(V)



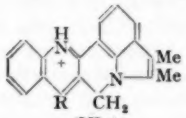
(VI)

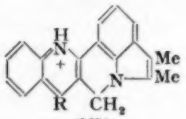
The keto-amine (II) readily formed a phenylhydrazone which in boiling ethanolic hydrogen chloride underwent the Fischer indolisation with the formation of a *ψ*-indole, *i.e.*, 4 : 5-dimethyl-*ψ*-indolo(2′ : 3′-1 : 2)liline (IV). The fact that during the reaction two hydrogen atoms have been lost with the formation of a *ψ*-indole rests on the following evidence : (*a*) the composition of the compound as determined by analysis, which differentiates sharply between the *ψ*-indole and the true indole, (*b*) infra-red analysis shows no –NH– band in the 3-μ region, which the true indole would of course possess, (*c*) the compound readily forms a stable crystalline hydrochloride, which does show the above –NH– band : this indicates that salt has the structure (V). *ψ*-Indoles (usually) exhibit this ready salt formation, particularly when (as in V) the process gives an aromatic character to each ring. It should be noted that simple salt formation at the liline nitrogen atom would not produce the above –NH– band. The *ψ*-indole (IV) also formed a crystalline methiodide, undoubtedly analogous to (V). In these properties the keto-amine (II) strongly resembles 1-ketojulolidine.

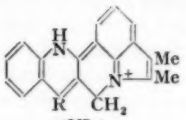
When the keto-amine (II) was heated with isatin in alkaline solution, subsequent acidification precipitated 4 : 5-dimethylquinolino(2′ : 3′-1 : 2)liline-4′-carboxylic acid (VI; R = CO_2H), which formed deep red crystals, but gave a bright yellow crystalline potassium salt. The acid (VI; R = CO_2H), when heated in a high vacuum, underwent decarboxylation to give 4 : 5-dimethylquinolino(2′ : 3′-1 : 2)liline (VI; R = H), which also formed bright yellow crystals, but gave a bright red crystalline hydrochloride.

These colour relations indicate strongly that the carboxylic acid (VI; R = CO_2H) must exist as a zwitter-ion, which will have the canonical forms (VI*a*—*c*; R = CO_2^-), and hence would almost certainly be intensely coloured. The anion of the potassium salt could not of course show these forms, and its structure must correspond almost entirely to that of the acid as depicted in (VI; R = CO_2^-) : hence its much paler and less intense colour. The amine (VI; R = H) must also have a structure identical with that of this anion (with of course the CO_2^- group replaced by H), and hence has the same colour as the potassium salt. The hydrochloride of the amine forms a cation which similarly will have three canonical forms corresponding to (VI*a*—*c*; R = H), and hence this hydrochloride has a colour almost identical with that of the free acid in the zwitter-ion form. [It is possible furthermore that some charge separation between nitrogen atoms occurs in the anion of the potassium salt and in the free amine (VI; R = H), the 1′-nitrogen taking a negative and the liline-nitrogen a positive charge; although this may be partly responsible for the pale

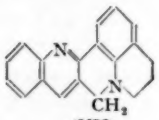
yellow colour, the separation is probably so small that it can be ignored.] The colour and structural relations of the acid (VI; R = CO_2H) and the base (VI; R = H) and their salts are thus very closely parallel to those of 1 : 2-dihydro-1-phenylquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid and its decarboxylated base (Mann, *J.*, 1949, 2816).

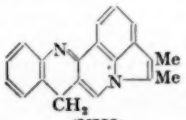

(VI*a*)

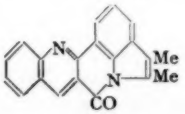

(VI*b*)


(VI*c*)

This provides reasonably strong (although indirect) evidence that the structure (VI; R = H) is correctly assigned to the decarboxylated base. The point is important because the structurally similar quinolino(2′ : 3′-1 : 2)juloline (VII) exists in two isomeric forms, one yellow and the other orange, the former giving a deep red, and the latter an orange hydrochloride (Mann and Smith, *loc. cit.*) : interconversion of the two series occurs readily, for the orange base on heating gives the yellow base, whilst the hydrochloride of the yellow base when boiled in aqueous solution is readily transformed into that of the orange base. It was suggested that the difference between the two series was possibly due to allylic tautomerism between the $C_{(3)}$ and the $C_{(4')}$ position.


(VII)


(VIII)


(IX)

It is clear that the liline base (VI; R = H) could theoretically also exist in a similar tautomeric form (VIII) : we have therefore very carefully investigated the properties of the base and its salts, but have not detected any signs of the existence of isomeric forms. The effect of the pyrrole ring is thus to give predominating stability to one of these forms, which is almost certainly that shown as (VI; R = H).

The amine (VI; R = H) showed one marked resemblance to the juloline base (VII) in that, when exposed in benzene solution to the air or when treated with a cold acetone solution of potassium permanganate, it underwent ready oxidation to 3-keto-4 : 5-dimethylquinolino(2′ : 3′-1 : 2)liline (IX). The fact that the base has undergone oxidation in the form (VI; R = H) and not (VIII), *i.e.*, that the keto-group occupies the 3- and not the 4′-position is hardly in doubt, since all previous similar oxidations have thus given rise to cyclic amides. It is noteworthy that the oxidation product (IX) forms cream-coloured crystals, but its hydrochloride is orange. This marked difference in the colour of the hydrochloride of the amine (VI; R = H) and that of the keto-compound (IX) is to be expected, because although the cation of the latter would also have three canonical forms corresponding in type to (VI*a*—*c*; R = H), the form corresponding to (VI*c*; R = H) would now make a much smaller contribution owing to the decrease in basicity of the liline-nitrogen atom caused by the adjoining 3-keto-group : hence this hydrochloride has a much less intense colour than that of the amine (VI; R = H).

We are now investigating the possibility of cyclising 1 : 2-dialkyl-3-2′-cyanoethylindoles, and the corresponding 2′-carboxyethyl compounds, in which a similar ring formation should occur at the 4-position.

Experimental.

Many of the following compounds did not give sharp and consistent m. p.s unless the material was heated in an evacuated and sealed capillary tube : all m. p.s so determined are denoted by an asterisk.

1-2′-*Cyanoethyl*-2 : 3-*dimethylindole*.—A mixture of 2 : 3-dimethylindole (50 g.), vinyl cyanide (89 g.), and sodium methoxide (1·8 g.) was heated in an autoclave at 160° for 12 hours, and then distillation furnished the *indole*, b. p. 182—185°/1 mm., which readily solidified and

when recrystallised from *cyclo*hexane formed colourless needles, m. p. 80° (39 g., 57%) (Found C, 78·3; H, 7·3; N, 14·0. $C_{13}H_{14}N_2$ requires C, 78·7; H, 7·1; N, 14·1%).

1-2′-*Carboxyethyl*-2 : 3-*dimethylindole*.—The cyano-indole (20 g.) was heated with 10% aqueous potassium hydroxide (300 c.c.) under reflux for 3 hours, and the whole then cooled, filtered, and acidified. The precipitated *acid* recrystallised from aqueous ethanol as colourless crystals which slowly became pink on exposure to light and had m. p. 96—97° (16·8 g., 77%) (Found : C, 71·4; H, 7·1; N, 6·4. $C_{13}H_{15}O_2N$ requires C, 71·8; H, 7·0; N, 6·45%).

1 : 2-*Dihydro*-1-*keto*-4 : 5-*dimethyl-liline* (II).—A mixture of the acid (10 g.), phosphoric anhydride (15 g.), fine silica powder (" Hyflo supercel ") (5 g.), and dry xylene (135 c.c.) was heated under reflux for 3 hours with vigorous stirring. The xylene was then decanted, and the residue extracted with boiling xylene (3 × 50 c.c.). The xylene was distilled from the united extracts, and the residue, when recrystallised from light petroleum (b. p. 60—80°), furnished the *keto-amine* (II) as yellow crystals, m. p. 98—99° (3 g., 30%) (Found : C, 78·25; H, 6·3; N, 7·0. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·6; N, 7·0%).

The *phenylhydrazone* readily crystallised when the keto-amine (II) (2 g.), phenylhydrazine (2 g.), acetic acid (1 c.c.), and ethanol (50 c.c.) were boiled together for 3 hours and then cooled : recrystallisation from ethanol gave yellow plates, m. p.* 165—166° (2·2 g., 75%) (Found : C, 79·1; H, 6·8; N, 14·5. $C_{19}H_{19}N_3$ requires C, 78·8; H, 6·6; N, 14·5%). The crystalline hydrazone when set aside slowly decomposed.

4 : 5-*Dimethyl-ψ-indolo*(2′ : 3′-1 : 2)*liline* (IV).—Saturated ethanolic hydrogen chloride (15 c.c.) was added to a mixture of the phenylhydrazone (1 g.) and ethanol (15 c.c.) which was then boiled under reflux for 45 minutes, crystals of the hydrochloride of (IV) separating meanwhile. These were collected from the cold mixture and dissolved in hot water, and the solution basified, bright yellow crystals of the *ψ-indolo-liline* (IV) then separating. These crystals (0·47 g., 52%), when recrystallised from methanol, had m. p.* 258° (Found : C, 84·4; H, 5·4; N, 10·4. $C_{19}H_{14}N_2$ requires C, 84·4; H, 5·2; N, 10·4%).

The addition of ethanolic hydrogen chloride to an ethanolic solution of (IV) precipitated the yellow crystalline *hydrochloride* (V), m. p.* 363—365° after recrystallisation from ethanol (Found : C, 74·6; H, 5·2; N, 9·2. $C_{19}H_{14}N_2$,HCl requires C, 74·4; H, 4·9; N, 9·1%).

When a solution of (IV) in an excess of methanolic methyl iodide was boiled for 3 hours, the orange crystalline *methiodide* was obtained, and after recrystallisation from methanol had m. p.* 362—363° (decomp.) (Found : C, 58·4; H, 4·5; N, 6·8. $C_{20}H_{17}N_2I$ requires C, 58·3; H, 4·2; N, 6·8%).

4 : 5-*Dimethylquinolino*(2′ : 3′-1 : 2)*liline*-4′-*carboxylic Acid* (VI; R = CO_2H).—A mixture of the keto-amine (II) (2 g.), isatin (2·6 g.), 30% aqueous potassium hydroxide (12 c.c.), and ethanol (50 c.c.) was boiled under reflux under nitrogen for 12 hours. The cold solution was poured into air-free water (150 c.c.) and acidified with 50% aqueous acetic acid. The *acid* was precipitated as a dark red oil which when set aside or (preferably) when heated in water, formed orange-red crystals (3 g., 91%). For purification the acid was dissolved in an excess of hot 20% aqueous potassium hydroxide, giving a yellow solution which on cooling deposited the potassium salt as bright yellow plates, which were recrystallised from 10% potassium hydroxide solution. This salt when treated with aqueous acetic acid deposited the deep red crystalline *hemihydrate*, m. p. 261—262° (effervescence), of the acid (Found : C, 75·0; H, 4·8; N, 8·3. $C_{21}H_{16}O_2N_2,\frac{1}{2}H_2O$ requires C, 74·7; H, 5·1; N, 8·3%). The potassium salt on exposure to damp air readily became red; it was unaffected by boiling methyl iodide.

4 : 5-*Dimethylquinolino*(2′ : 3′-1 : 2)*liline* (VI; R = H).—When the acid (VI; R = CO_2H) (1 g.) was heated at 320°/0·1 mm. for 1 hour, the *amine* sublimed and when then recrystallised from much ethanol formed bright yellow needles, m. p.* 208° (0·7 g., 81%) (Found : C, 84·6; H, 5·6; N, 10·0. $C_{20}H_{16}N_2$ requires C, 84·4; H, 5·7; N, 9·9%).

When ethanolic hydrogen chloride was added to an ethanolic solution of the amine (VI; R = H), the red *hydrochloride* was precipitated; when recrystallised from ethanol this formed bright red needles, m. p.* 302—304° (Found : C, 74·9; H, 5·5; N, 8·65. $C_{20}H_{16}N_2$,HCl requires C, 74·9; H, 5·3; N, 8·7%).

The formation of this salt under various conditions, and particularly its behaviour when heated with hydrochloric acid and other solvents, were carefully investigated, but no evidence of any change to an isomeric form, similar to that shown by the hydrochloride of quinolino-(2′ : 3′-1 : 2)juloline (VII), could be obtained.

3-*Keto*-4 : 5-*dimethylquinolino*(2′ : 3′-1 : 2)*liline* (IX).—(*a*) A cold acetone solution of potassium permanganate was added with stirring to a solution of the amine (VI; R = H) (0·4 g.) in acetone (200 c.c.) until the latter retained a purple colour. The precipitated

manganese dioxide, which contained almost all the oxidation product, was collected and extracted (Soxhlet) with acetone (50 c.c.). The 3-*keto-liline* (IX) separated from the hot acetone, and when cold was collected and recrystallised from 2-methoxyethanol, furnishing very pale yellow (almost cream) needles, m. p.* 251—252° (0·3 g., 71%) (Found: C, 80·6; H, 5·0; N, 9·2. $C_{20}H_{14}ON_2$ requires C, 80·5; H, 4·7; N, 9·4%).

(*b*) A benzene solution of the amine (VI; R = H) was exposed to air for 7 days and then evaporated. Recrystallisation of the residue as before gave pale yellow needles, m. p.* 250—251°, alone and when mixed with the above sample.

The finely powdered amine (VI; R = H) was virtually unaffected by exposure to a stream of air at 120° for 10 hours.

When ethanolic hydrogen chloride was added to a cold acetone solution of (IX), the *hydrochloride* was precipitated as orange crystals which had m. p.* 251° and hence had apparently completely dissociated before reaching the m. p. of the base (Found: C, 71·8; H, 4·8; N, 8·35. $C_{20}H_{14}ON_2$,HCl requires C, 71·8; H, 4·5; N, 8·4%).

We are greatly indebted to Dr. R. N. Haszeldine for the spectroscopic investigation, to the Department of Scientific and Industrial Research for a grant (to C. Y. A.), and to Imperial Chemical Industries Limited, Dyestuffs Division, for the gift of various compounds.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 22nd,* 1952.]

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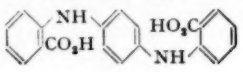
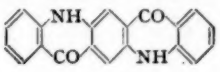
344. *Polynuclear Heterocyclic Systems. Part V.** 5:8-*Diazapentaphene.*

By G. M. BADGER and R. PETTIT.

Cyclisation of *p*-phenylenedianthranilic acid (I) has been shown to give the angular quinacridone (III). The aza-hydrocarbon prepared from this is 5:8-diazapentaphene (VIII) and not the linear compound (IV), from (II), as originally supposed by Ullmann and Maag (*Ber.*, 1907, **40**, 2515). Oxidation of diazapentaphene (VIII) with selenium dioxide gave 2:3-6:7-dibenzo-1:8-diazafluorenone (XII).

IN 1907, Ullmann and Maag (*Ber.*, 1907, **40**, 2515; see also *Ber.*, 1906, **39**, 1693) described the preparation of *NN'-p*-phenylenedianthranilic acid (I) and its cyclisation to a "quinacridone." The direction of cyclisation was not established, but the linear structure (II) was favoured rather than the alternative angular compound (III). The supposed (II) was reduced to a red dihydro-compound, and on mild oxidation this gave an aromatic aza-hydrocarbon which was thought to be the linear pentacyclic compound (IV). On the other hand, by treating *p*-benzoquinone with anthranilic acid, followed by cyclisation of


(I)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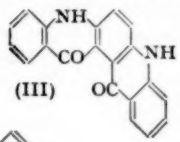
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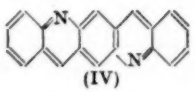
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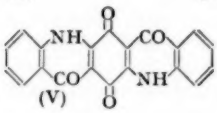
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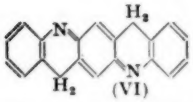
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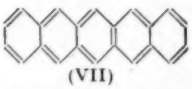

(VII)

the product, Leśniański (*Ber.*, 1918, **51**, 695) obtained a compound having the structure (V). On zinc-dust distillation, this gave a very small amount of a dark red dihydro-compound (presumably VI †) which was not identical with Ullmann and Maag's dihydro-derivative.

* Part IV, 1951, 3211.

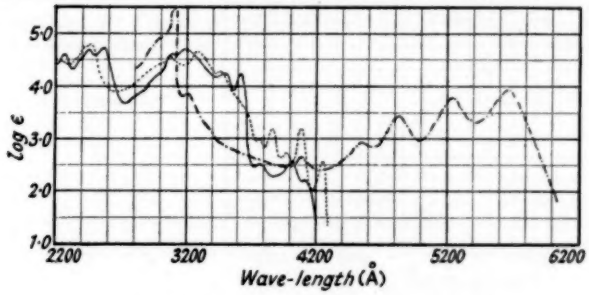
† The red colour of this compound indicates that it must have a completely conjugated quinonoid structure (cf. Badger and Pettit, *J.*, 1951, 3211). The alternative structure favoured by Leśniański would have an acridine-like spectrum and would be yellow.

He therefore suggested that the compound obtained by Ullmann and Maag must have an angular structure. Furthermore, by cyclisation of 2:5-dianilinoterephthalic acid, Liebermann (*Annalen*, 1935, **518**, 245) prepared authentic linear quinacridone (II) and found it to be different from the quinacridone obtained by Ullmann and Maag.

In view of these discrepancies, it seemed certain that Ullmann and Maag's aza-hydrocarbon could not have the structure (IV), and this conclusion is supported by other evidence. It has been shown (Badger, Pearce, and Pettit, *J.*, 1951, 3199) that the absorption spectra of aromatic heterocyclic compounds closely resemble those of their carbocyclic analogues. This means that the colour of an unknown aromatic heterocyclic compound can be predicted with reasonable certainty provided the analogous hydrocarbon is known. It is therefore significant that, although the aromatic hydrocarbon pentacene (VII) is deep blue, Ullmann and Maag's aromatic heterocylic compound is pale yellow.

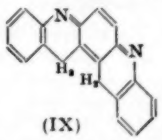
It has now been found that cyclisation of *p*-phenylenedianthranilic acid (I) gives the angular quinacridone (III), and that the aromatic compound derived from it is 5:8-diazapentaphene (VIII). Its absorption spectrum (Fig. 1) resembles that of the analogous

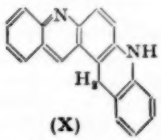
FIG. 1. *Absorption spectra of* 5:8-*diazapentaphene* (– – – – –), *of pentaphene* (———), *and of pentacene* (·—·—·—), *all in ethanol. The spectra of the two hydrocarbons are taken from Clar* (Ber., 1932, **65**, 503; "*Aromatische Kohlenwassertsoffe*," *Springer-Verlag*, 1941, *p.* 182).



hydrocarbon, pentaphene, very closely indeed, and such differences as are found are in the direction expected (cf. Badger, Pearce, and Pettit, *loc. cit.*). On the other hand, the spectrum differs widely from that of the linear hydrocarbon, pentacene (VII). The red

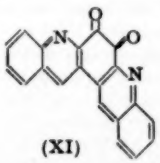
(VIII)

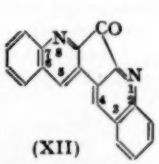

(IX)

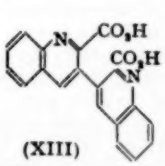

(X)

colour of the intermediate dihydro-compound indicates that this substance must have a completely conjugated quinonoid structure (IX), and not the alternative form (X).

It was hoped to confirm the structure of the diazapentaphene (VIII) by oxidation to the *o*-quinone (XI) and subsequent condensation with *o*-phenylenediamine. Unfortunately


(XI)


(XII)


(XIII)

the aza-hydrocarbon proved very resistant to oxidation, even to chromic acid in concentrated sulphuric acid, and the desired quinone could not be obtained.

With selenium dioxide in a sealed tube, oxidation proceeded readily. However, the

analysis and absorption spectrum of the product indicate that it must be 1 : 8-diaza-2 : 3-6 : 7-dibenzofluorenone (XII), and it seems likely that this is formed from the aza-hydrocarbon (VIII) by oxidation to the quinone (XI), then to the dicarboxylic acid (XIII), and subsequent loss of carbon dioxide and water. Fig. 2 shows the absorption spectrum of 1 : 8-diaza-2 : 3-6 : 7-dibenzofluoreneone and that of the " parent " substance, 2 : 3-6 : 7-dibenzofluorenone, which was prepared by Martin's method (*J.*, 1941, 679). Diazabenzofluorenone (XII) could only arise by oxidation of the angular aza-hydrocarbon (VIII), and this fact confirms this assignment of structure to the compound originally prepared by Ullmann and Maag.

Little difficulty was experienced in repeating Ullmann and Maag's synthesis; but some improvements are recorded in the Experimental section. The reduction of the quinacridone (III) with sodium and alcohol gave the dihydro-compound (IX) together with a colourless product (also noted by the original workers) which has been identified as acridan. The presence of this material is due to the incomplete removal of *N*-*p*-bromophenylanthranilic acid from the *p*-phenylenedianthranilic acid (I) before cyclisation. This leads to the presence of 3-bromoacridone in the quinacridone, and on reduction this yields

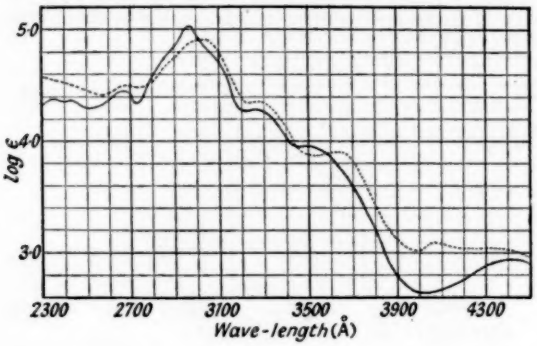


FIG. 2. *Absorption spectra of* 2 : 3-6 : 7-*dibenzofluorenone* (———), *and of* 1 : 8-*diaza*-2 : 3-6 : 7-*dibenzofluorenone* (– – – –), *both in ethanol.*

acridan. This impurity was largely eliminated by using a large excess of anthranilic acid in the preparation of *p*-phenylenedianthranilic acid.

EXPERIMENTAL

NN'-p-*Phenylenedianthranilic Acid* (I).—A mixture of anthranilic acid (140 g.), potassium carbonate (100 g.), *p*-dibromobenzene (70 g.), cuprous chloride (2·7 g.), copper bronze (1·8 g.), and *iso*amyl alcohol (120 c.c.) was heated in an oil-bath at 150° for 3½ hours. After steam-distillation, the mixture was filtered and acidified with hydrochloric acid, and the precipitate collected. After extraction with boiling ethanol (6 × 300 c.c.) the *p*-phenylenedianthranilic acid (90 g.) was obtained as pale greenish-yellow crystals, m. p. 290—292° (Ullmann and Maag give m. p. 286°).

From the alcoholic liquors, *N*-*p*-bromophenylanthranilic acid (15 g.) was obtained as colourless plates, m. p. 182—183°.

13 : 14-*Dihydro*-5 : 8-*diazapentaphene.*—Cyclisation of the above *p*-phenylenedianthranilic acid (60 g.) was carried out essentially as described by Ullmann and Maag (*loc. cit.*), and yielded the quinacridone (III) (32 g.) as pale yellow needles, m. p. 412—414° (Ullmann and Maag give m. p. 394°). For the reduction, the quinacridone (8 g.) in boiling absolute alcohol (240 c.c.) was treated with sodium (24 g.) in small pieces. The mixture was then evaporated on a steam-bath, with constant stirring, to a thick red paste. This paste was added to a mixture of 10N-hydrochloric acid (120 c.c.) and water (200 c.c.), and the dark blue precipitate of the hydrochloride was collected and washed. The free base (4·0 g.) was obtained by addition to aqueous ammonia, and on recrystallisation from alcohol, the 13 : 14-dihydro-5 : 8-diazapentaphene formed deep-red needles, m. p. 243°. Solutions of this compound were oxidised in air to the aromatic substance.

5 : 8-*Diazapentaphene.*—This was obtained by oxidation of the above dihydro-compound

with nitric acid in acetic acid. It crystallised from alcohol in pale yellow needles, m. p. 245°, in agreement with Ullmann and Maag.

Acridan.—Cyclisation of *N*-*p*-bromophenylanthranilic acid (10 g.) with sulphuric acid in the same manner as for *p*-phenylenedianthranilic acid, gave 3-bromoacridone (6 g.), which formed yellow needles, m. p. 389° (decomp.), from acetic acid. Reduction of this compound (2 g.) with sodium and boiling alcohol gave a colourless product (1·4 g.) which, after recrystallisation from alcohol, formed colourless needles, m. p. 167—168° alone or mixed with an authentic specimen of acridan. Its identification was completed by oxidation, with potassium dichromate in acetic acid, to acridine, m. p. and mixed m. p. 111—112°.

1 : 8-*Diaza*-2 : 3-6 : 7-*Dibenzofluorenone.*—A mixture of 5 : 8-diazapentaphene (2·0 g.), selenium dioxide (4·0 g.), and water (15 c.c.) was heated in a sealed tube at 230—240° for 4 hours. After the mixture had cooled, the product was collected, washed well with water, and dried. The resulting yellow powder was first heated at 180°/0·01 mm. for 30 minutes to remove selenium; the residue was then sublimed at 240—250°/0·01 mm., the sublimate being collected. 1 : 8-*Diaza*-2 : 3-6 : 7-*dibenzofluorenone* (1·0 g.) was recrystallised from pyridine, and formed beautiful orange needles, m. p. 374—376° (Found: C, 81·1; H, 3·75; N, 9·8. $C_{19}H_{10}ON_2$ requires C, 80·8; H, 3·6; N, 9·9%).

2 : 3-6 : 7-*Dibenzofluorenone.*—Prepared by Martin's method (*loc. cit.*), this had m. p. 277—278°.

Absorption Spectra.—These were determined with a Hilger Uvispek spectrophotometer.

We are indebted to the Commonwealth Government Research Fund for a maintenance grant (to R. P.). Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne.

UNIVERSITY OF ADELAIDE. [*Received, December 28th*, 1951.]

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345. *Polynuclear Heterocyclic Systems. Part VI.* Tetra-azabenzopentaphene and Related Compounds.*

By G. M. BADGER and R. PETTIT.

Unlike the linear compound (I), the tetra-azabenzopentaphene (VII) does not form a stable dihydride.

The supposed dihydride reported by Kehrmann (*Ber.*, 1923, **56**, 2390) has been shown to be 14-*o*-aminophenyl-13 : 14-dihydro-5 : 8 : 13 : 14-tetra-aza-6 : 7-benzopentaphene (XI). Some reactions of this compound have been investigated.

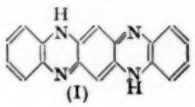
IN Part IV of this series (Badger and Pettit, *J.*, 1951, 3211), it was pointed out that the linear pentacyclic compound "homofluorindine" (5 : 12-dihydro-5 : 7 : 12 : 14-tetra-azapentacene) must have the *p*-quinonoid type of structure (I). Its deep blue-purple colour and its absorption spectrum support such a formulation, and exclude the alternative structure (II) which could not have the observed spectrum or be so deeply coloured. The remarkable stability of this quinonoid dihydro-compound is of some theoretical importance.

As we are investigating the relation between aromatic hydrocarbons and their heterocyclic analogues, we examined another compound which could exist in a similar quinonoid structure, *viz.*, the dihydro-derivative of 5 : 8 : 13 : 14-tetra-aza-6 : 7-benzopentaphene. Of the three possible structures for this, namely (III), (IV), and (V), the *p*-quinonoid structure (V) would be preferred by analogy with "homofluorindine" (I). Structure (V), involving complete conjugation through the molecule, would be more stable than the *o*-quinonoid structure (IV), or the alternative form (III) having two isolated conjugated systems.

A dihydro-derivative of tetra-azabenzopentaphene purporting to be (III) was reported by Kehrmann (*Ber.*, 1923, **56**, 2390); but further investigation shows that it does not have this structure (see below).

* Part V, preceding paper.

Many attempts have been made to obtain an authentic specimen of the dihydride (III, IV, or V). When 1 : 2-benzophenazine-3 : 4-quinone (VI) is condensed with *o*-phenylenediamine, it gives the parent aromatic substance, 5 : 8 : 13 : 14-tetra-aza-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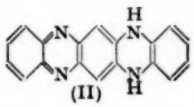
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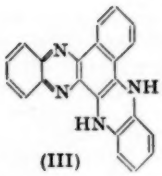
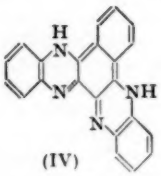

(III)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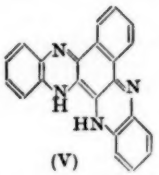
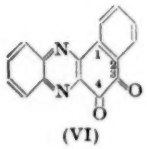
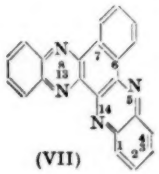

(V)

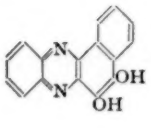
6 : 7-benzopentaphene (VII) (Zincke and Wiegand, *Annalen*, 1895, **286**, 58), and it was thought that similar condensation of 3 : 4-dihydroxy-1 : 2-benzophenazine (VIII) with *o*-phenylenediamine would give the desired dihydride. In fact, however, spontaneous oxidation occurred and only the aza-hydrocarbon (VII) was obtained.

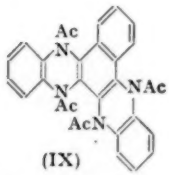
Attempts to obtain the dihydride by catalytic reduction of the aza-hydrocarbon (VII) were also unsuccessful. Hydrogen was absorbed, and a colourless solution was obtained; but on filtration to remove the catalyst, the solution rapidly became red, and later was oxidised to the original tetra-azabenzopentaphene.

Reductive acetylation of tetra-azabenzopentaphene proceeded normally, and a tetra-acetyl derivative (IX) was obtained. On hydrolysis with alcoholic potash or with sulphuric acid, however, this again reverted to the aza-hydrocarbon (VII). When the tetra-acetyl derivative was treated with sulphuric acid for 15 seconds and then immediately poured into water a red compound, probably (V), was obtained; but it was very unstable. It was very readily oxidised to tetra-azabenzopentaphene (VII) with nitric acid, and its


(VI)


(VII)

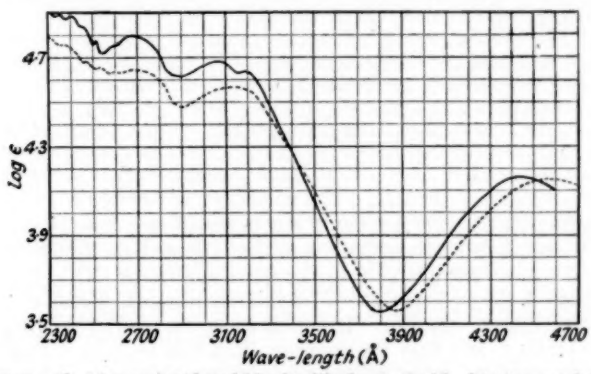

(VIII)


(IX)

alcoholic solutions were also rapidly oxidised in air. A completely pure specimen could not be obtained. It must be concluded, therefore, that although tetra-azabenzopentaphene does form a dihydride, this readily reverts to the more stable aromatic compound. This system is therefore not comparable with the remarkably stable "homofluorindine" (I). In this respect, it is also noteworthy that the angular compound 13 : 14-dihydro-5 : 8-diazapentaphene is also unstable, its solutions being rapidly oxidised in air (see Part V, *loc. cit.*).

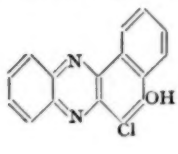
Kehrmann's supposed dihydride was prepared by condensation of 4-chloro-3-hydroxy-1 : 2-benzophenazine (X) with *o*-phenylenediamine in molten naphthalene. This reaction has now been shown to give three products. The first, also obtained by Kehrmann, was a dark blue-purple powder having no melting point. It was identified as "homofluorindine" (I) by reductive acetylation to 5 : 7 : 12 : 14-tetra-acetyl-5 : 7 : 12 : 14-tetrahydro-5 : 7 : 12 : 14-tetra-azapentacene and direct comparison with an authentic specimen. Its formation is due to atmospheric oxidation of the *o*-phenylenediamine (Badger and Pettit, *J.*, 1951, 3211). The second substance, which was not isolated by Kehrmann, crystallised from acetic acid in pale yellow needles, and was identified as 5 : 8 : 13 : 14-tetra-azapentaphene (VII). It is evidently formed by atmospheric oxidation of the dihydride (III), the expected product of the reaction. The third compound crystallised

from chloroform in yellow-orange plates, and was clearly identical with the substance isolated by Kehrmann and to which he assigned the structure (III). Repeated analyses, however, showed that it could not have this formula, and the structure (XI; R = H) is now proposed for it. It formed a stable dark red hydrochloride without difficulty, and was a moderately strong base. On oxidation with hydrogen peroxide, it gave tetra-aza-benzopentaphene (VII). It gave an alkali-soluble toluene-*p*-sulphonyl derivative (XI; R = $SO_2 \cdot C_6H_4Me$) which confirmed the presence of the primary amino-group, and, with

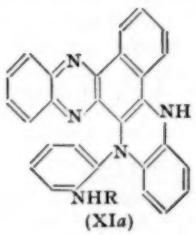


Absorption spectrum of 14 *o-aminophenyl-*13 : 14*-dihydro-*5 : 8 : 13 : 14*-tetra-aza-*6 : 7*-benzopentaphene* (XI) *in dioxan* (———) *and in* 50% *aqueous dioxan* (– – – –). *In the latter solvent, the long-wave-length absorption band is shifted nearly* 200 Å *to longer wave-lengths.*

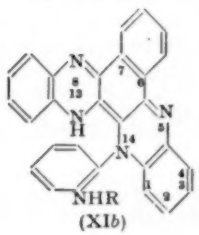
acetyl chloride, a monoacetyl derivative (XI; R = Ac). Attempted acetylation with acetic anhydride, however, gave a colourless oxygen-free compound, which seems to be (XIII). Such a compound could arise by acetylation of the imino-nitrogen atom to give the intermediate (XII), and subsequent transannular elimination of water.



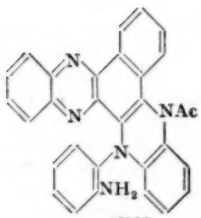
(X)



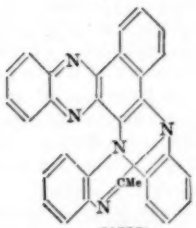
(XI*a*)



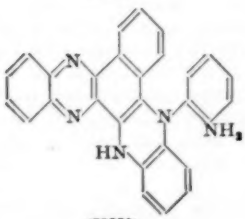
(XI*b*)



(XII)



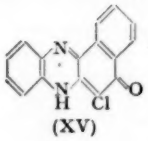
(XIII)

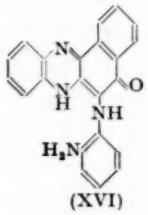


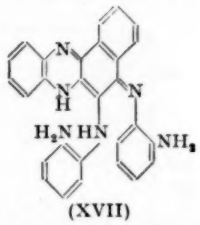
(XIV)

These reactions do not distinguish between structures (XI) and (XIV), but the former is preferred for spectrographic reasons. Solutions of the free base (XI; R = H), of the acetyl derivative (XI; R = Ac), and of the sulphonamido-derivative (XI; R = $SO_2 \cdot C_6H_4Me$), in pure dioxan, are all pale yellow; but on the addition of water there is a pronounced deepening of colour. This is illustrated by the two absorption curves of the free base (see figure). The increase in depth of colour with increase in the dielectric constant

of the solvent can only be associated with the tautomeric change (XI*a*) ⟶ (XI*b*), the quinonoid form being favoured by high dielectric constant. Similar tautomeric shifts are known to occur with 2-hydroxyacridine and 2-hydroxyphenazine (Albert and Short, *J.*, 1945, 760; Badger, Pearce, and Pettit, *J.*, 1951, 3204). Such changes do not occur with the 1-hydroxy-compounds, and a similar tautomeric shift would not be expected with structure (XIV).


(XV)


(XVI)


(XVII)

The mechanism of the reaction leading to Kehrmann's compound (XI) is also of interest. In this respect, it seems to be important that the intermediate 4-chloro-3-hydroxy-1 : 2-benzophenazine (X) must exist largely in the quinonoid form (XV), for it is a deep red compound (compare 4-chloro-3-methoxy-1 : 2-benzophenazine, which is yellow; see also Badger, Pearce, and Pettit, *loc. cit.*). It therefore seems likely that this compound will react as a chloroquinone, and that the chlorine atom will be very readily substituted by an amino-group to give the intermediate basic quinone (XVI). Such an intermediate could react in two ways. If the quinone group condenses with the second amino-group of the *o*-phenylenediamine moiety, the unstable dihydride (III) would be formed and would rapidly oxidise to the fully aromatic aza-hydrocarbon (VII) actually isolated from the reaction mixture. On the other hand, if the intermediate basic quinone (XVI) condenses with a second *o*-phenylenediamine molecule, the diamino-compound (XVII) would be formed, and at the high reaction temperature, this would be expected to eliminate ammonia and give (XI; R = H).

This scheme is supported by the fact that the pale yellow isomeric compound 3-chloro-4-hydroxy-1 : 2-benzophenazine, which does not exist in a quinoid form (cf. 1-hydroxyphenazine; Badger, Pearce, and Pettit, *loc. cit.*), condenses with *o*-phenylenediamine to give tetra-azabenzopentaphene (VII) alone. Kehrmann's compound (XI) could not be obtained from this reaction.

Experimental

5 : 8 : 13 : 14-*Tetra-aza*-6 : 7-*benzopentaphene*.—1 : 2-Benzophenazine was prepared from *o*-phenylenediamine and 1-nitroso-2-naphthol by Ullmann and Heisler's method (*Ber.*, 1909, **42**, 4263). Oxidation to the 3 : 4-quinone (VI) was achieved with chromic acid in acetic anhydride–acetic acid (Fischer and Schindler, *Ber.*, 1906, **39**, 2238). A solution of 1 : 2-benzophenazine-3 : 4-quinone (0·5 g.) in acetic acid (200 c.c.) was treated with *o*-phenylenediamine (1·0 g.) in a little alcohol, and the mixture boiled for 10 minutes. After cooling, the product (0·65 g.) was collected and recrystallised from glacial acetic acid. 5 : 8 : 13 : 14-Tetra-aza-6 : 7-benzopentaphene (VII) formed very pale yellow needles, m. p. 320—321° (Found: C, 79·2; H, 3·7. Calc. for $C_{22}H_{12}N_4$: C, 79·5; H, 3·6%). Zincke and Wiegand (*Annalen*, 1895, **286**, 58) report the m. p. as "above 275°." This substance electrifies very readily on being rubbed.

The same substance was also obtained when a mixture of 3 : 4-dihydroxy-1 : 2-benzophenazine (0·3 g.) (Badger, Pearce, and Pettit, *loc. cit.*) and *o*-phenylenediamine (1·0 g.) in ethyl acetate (20 c.c.) was boiled under reflux for 6 hours. The solution, which was initially blue, gradually became red-brown, and the pale yellow crystals of tetra-azabenzopentaphene separated in almost quantitative yield on cooling.

5 : 8 : 13 : 14-*Tetra-acetyl*-5 : 8 : 13 : 14-*tetra-aza*-5 : 8 : 13 : 14-*tetrahydro*-6 : 7-*benzopentaphene*.—The above tetra-azabenzopentaphene was boiled with zinc dust and acetic anhydride, containing a little anhydrous sodium acetate. The solution immediately became deep green, but became colourless on further heating. After 3 hours, the solution was filtered from the

excess of zinc and poured into water. The *tetra-acetyl* derivative (IX) formed small colourless prisms, m. p. 318° (Found: C, 71·1; H, 4·8. $C_{30}H_{24}O_4N_4$ requires C, 71·4; H, 4·8%).

Hydrolysis of this (0·5 g.) with boiling 5% alcoholic potash (50 c.c.) immediately gave a green solution. After 30 minutes, the solid was collected and identified as 5 : 8 : 13 : 14-tetra-aza-6 : 7-benzopentaphene by its m. p. and mixed m. p.

Hydrolysis with concentrated sulphuric acid for 5 minutes likewise gave the tetra-azabenzopentaphene. The crude dihydride (V) was obtained as follows. Finely powdered tetra-acetyl compound (IX) was quickly added to concentrated sulphuric acid, with vigorous stirring. After 15 seconds the mixture was poured into a large volume of water, and the precipitate collected. After being washed with a little water it was stirred into aqueous ammonia, and the resulting crude dihydride collected. This material always contained some tetra-azabenzopentaphene, and no purification could be effected by recrystallisation. Alcoholic solutions exposed to air rapidly oxidised completely to tetra-azabenzopentaphene, and immediate oxidation was also brought about by addition of a little nitric acid to an acetic acid solution. The crude red material gave blue solutions with sulphuric, hydrochloric, and acetic acids.

Preparation of Kehrmann's Compound (XI; R = H).—A mixture of 4-chloro-3-hydroxy-1 : 2-benzophenazine (12 g.), *o*-phenylenediamine (7·1 g.), and naphthalene (75 g.) was heated at 210—215° on a sand-bath for 20 minutes with continuous stirring. After removal of the naphthalene by steam-distillation, the residue was dried, powdered, and then heated under reflux for 30 minutes with chloroform (1000 c.c.). After filtration, the residue was similarly treated with a further quantity (300 c.c.) of chloroform. The dark blue-purple residue was identified as " homofluorindine " (I) by reductive acetylation. After recrystallisation from nitrobenzene, it formed colourless crystals, m. p. 375—376°, identical with 5 : 7 : 12 : 14-tetra-acetyl-5 : 7 : 12 : 14-tetrahydro-5 : 7 : 12 : 14-tetra-azapentacene (Badger and Pettit, *loc. cit.*).

The combined chloroform filtrates were concentrated to 350 c.c. and kept overnight. The material which separated (4·5 g.) was collected. After recrystallisation from chloroform, the 14-*o*-*aminophenyl*-13 : 14-*dihydro*-5 : 8 : 13 : 14-*tetra*-*aza*-6 : 7-*benzopentaphene* (XI; R = H) formed beautiful golden plates, m. p. 272° (Found: C, 78·6; H, 4·9; N, 16·15. $C_{28}H_{19}N_5$ requires C, 79·0; H, 4·5; N, 16·45%). It was also obtained in orange needles of the same m. p. by recrystallisation from alcohol–benzene. It dissolved in alcohol and in dioxan to give orange-yellow solutions, which became distinctly red on dilution. It gave a deep green solution in concentrated sulphuric acid, which became red on dilution. With concentrated hydrochloric acid, it gave the *dihydrochloride*. On recrystallisation from aqueous alcohol, this formed deep red glistening plates, m. p. 285—286° (Found: C, 64·9; H, 4·65. $C_{28}H_{19}N_5,2HCl,H_2O$ requires C, 65·1; H, 4·5%).

After removal of Kehrmann's compound, the chloroform liquors were concentrated to 100 c.c., and again set aside. After 12 hours, the 5 : 8 : 13 : 14-tetra-aza-6 : 7-benzopentaphene (4·2 g.) was collected. Recrystallisation from acetic acid gave pale yellow needles, m. p. and mixed m. p. 320°.

Acetylation of Kehrmann's Compound.—Acetylation of the above base (XI; R = H) was effected with acetyl chloride in pyridine. After recrystallisation from alcohol, the *acetyl* derivative (XI; R = Ac) formed fine yellow needles, m. p. 250—252° (slow heating) (Found: C, 73·8; H, 5·3; N, 13·0. $C_{30}H_{21}ON_5,1\frac{1}{4}C_2H_5{\cdot}OH$ requires C, 73·9; H, 5·6; N, 13·0%). It gave a yellow-orange solution in dioxan, becoming red on addition of water. With concentrated sulphuric acid, it gave a green solution, becoming red on dilution with water. It also gave a red solution with hydrochloric acid.

Action of Acetic Anhydride.—Brief boiling with acetic anhydride converted Kehrmann's compound (XI; R = H) into the substance (XIII). After recrystallisation from pyridine, this formed pale yellow plates, m. p. 266° (Found: C, 79·9; H, 4·2; N, 15·1. $C_{30}H_{19}N_5$ requires C, 80·2; H, 4·3; N, 15·6%).

Formation of Toluene-p-*sulphonyl Derivative.*—Treatment of Kehrmann's compound with toluene-*p*-sulphonyl chloride in dry pyridine gave the *toluene*-p-*sulphonyl* derivative (XI; R = $SO_2{\cdot}C_6H_4Me$). After recrystallisation from alcohol, it formed orange prisms, m. p. 228—229° (after slow heating to remove solvent of crystallisation) (Found, after drying at room temperature for several days: C, 69·8; H, 5·3; N, 10·2. $C_{35}H_{25}O_2N_5S,2C_2H_5{\cdot}OH$ requires C, 69·7; H, 5·5; N, 10·4%. Found, after drying at 110°/0·1 mm. for 8 hours: C, 70·8; H, 4·7; N, 11·25. $C_{35}H_{25}O_2N_5S,C_2H_5{\cdot}OH$ requires C, 71·0; H, 5·0; N, 11·2%).

Oxidation of Kehrmann's Compound with Hydrogen Peroxide.—A solution of Kehrmann's compound (XI; R = H) (0·1 g.) in acetic acid (10 c.c.) was treated with hydrogen peroxide (10 c.c.; 100-vol.), and the mixture kept for 2 days. After addition of water the product was

collected and recrystallised from acetic acid. The tetra-azabenzopentaphene formed pale yellow needles, m. p. and mixed m. p. 320°.

Preparation of Tetra-azabenzopentaphene from 3-Chloro-4-hydroxy-1 : 2-benzophenazine.—A mixture of the phenazine (10 g.) (Zincke, *Annalen*, 1891, **268**, 257; Zincke and Noak, *ibid.*, 1896, **295**, 6), *o*-phenylenediamine (8 g.), and naphthalene (60 g.) was heated on a sand-bath at 210—215° for 20 minutes. After removal of the naphthalene by steam-distillation and subsequent washing with light petroleum (200 c.c.), the dark brown residue (12 g.) was refluxed for 1 hour with chloroform (1300 c.c.), and then filtered off. The residue (5 g.) was identified as homofluorindine (I). Concentration of the liquors to 200 c.c. and storage overnight gave 5 : 8 : 13 : 14-tetra-aza-6 : 7-benzopentaphene (4·5 g.) as light yellow needles, m. p. and mixed m. p. 320°.

3-Acetoxy-4-chloro-1 : 2-benzophenazine.—This was prepared from the free hydroxy-compound (Kehrmann, *loc. cit.*) by 2 hours' boiling with excess of acetic anhydride. After recrystallisation from acetic acid, the *acetoxy*-compound formed yellow needles, m. p. 230—232°, after sintering (Found: C, 66·6; H, 3·4. $C_{18}H_{11}O_2N_2Cl$ requires C, 67·0; H, 3·4%).

4-Chloro-3-methoxy-1 : 2-benzophenazine.—This *methoxy*-compound was prepared in the usual way from the hydroxy-compound, with methyl sulphate. After recrystallisation from alcohol, it formed yellow needles, m. p. 177—178° (Found: C, 69·4; H, 3·7. $C_{17}H_{11}ON_2Cl$ requires C, 69·3; H, 3·8%).

Absorption Spectra.—These were determined with a Hilger Uvispek spectrophotometer.

We are indebted to the Commonwealth Government Research Fund for a maintenance grant (to R. P.). Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne.

UNIVERSITY OF ADELAIDE. [*Received, December 28th*, 1951.]

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346. *Magnetochemistry of the Heaviest Elements. Part VI.** PuO_2–ThO_2 *and* PuF_4–ThF_4 *Solid Solutions.*

By J. K. DAWSON.

The magnetic susceptibilities of plutonium dioxide and tetrafluoride have been measured over the temperature range 90—450° K. The tetrafluoride obeys the Curie–Weiss law above 200° K but there is an upward curvature below that temperature. Measurements on solid solutions of the tetrafluoride in isomorphous thorium tetrafluoride lead to an extrapolated susceptibility at infinite dilution in agreement with a $5f^4$ electron configuration.

The susceptibility of the dioxide does not obey the Curie–Weiss law and is considerably lower than that of the tetrafluoride, but dilution in thorium dioxide shows that the susceptibility increases very rapidly between 10 atomic % and infinite dilution. The intercept at infinite dilution appears to be about the value for a $5f^4$ configuration, but some of the evidence may indicate that $6d$ levels are occupied.

ON the basis of magnetic susceptibility measurements at temperatures about 76°, 190°, and 300° K, Elliott and Lewis reported that $Rb_4Pu(SO_4)_4,2H_2O$ obeys the Curie–Weiss law, but that PuF_4 and $Pu(C_2O_4)_2,6H_2O$ show an upward curvature and $Pu(SO_4)_2,4H_2O$ shows a downward curvature away from this law [Paper 90, Symposium: Chemistry of the Actinide Elements, American Chemical Society Meeting, Chicago, September, 1950]. They noted that the observed moments were abnormally lower than the theoretical one for a $5f^4$ electron configuration but that quenching of the orbital contribution would not account for the discrepancy.

Previous experiments on uranium dioxide and tetrafluoride have shown that the technique of dilution in solid solution with an isomorphous diamagnetic compound and extrapolation of the susceptibilities to infinite dilution provides a means for better assess-

* Part V, *J.*, 1952, 1185.

ment of the electron configuration, the result being not necessarily the one expected on the basis of measurements on the undiluted compounds (Trzebiatowski and Selwood, *J. Amer. Chem. Soc.*, **1950, 72,** 4505; Dawson, *J.*, 1952, 1185). This paper describes the results obtained by applying the same technique to plutonium dioxide and tetrafluoride.

Experimental

A stock solution of plutonium tetranitrate in dilute nitric acid was found by spectrographic analysis to contain negligible amounts of other elements, and the purity determined by counting and weighing an aliquot portion evaporated on to platinum foil was 100·8±2%. The absence of ferromagnetic impurities was checked further by susceptibility measurements at room temperature on the solid solutions at three field strengths: no dependence on field strength was observed.

Spectrographic analysis of a stock solution of thorium nitrate also showed negligible impurities, and a sample of thorium tetrafluoride prepared from it was found to be diamagnetic.

Aliquot portions of the plutonium and thorium nitrate solutions were mixed in quartz centrifuge tubes and the hydroxides were precipitated by addition of ammonium hydroxide. For the preparation of the oxides the tubes were centrifuged, the supernatant liquid was removed, and the tubes were placed in an oven the temperature of which was raised slowly to about 800° c. The tetrafluoride solid solutions were prepared by slurrying the hydroxides into a platinum boat which was heated to 450° c in a stream of hydrogen fluoride and oxygen in a copper furnace.

X-Ray diffraction patterns of the resulting oxides and fluorides showed that true solid solutions had been obtained. A plot of sin θ against composition for several of the most sharply defined lines showed that the plutonium percentages in the solid solutions were the same as those calculated from the amounts of stock solution taken, within the error of the measurements.

The samples (5—15 mg.) were enclosed in Pyrex capillaries and the measurements were made on the balance described in Part I of this series (Dawson and Lister, *J.*, 1950, 2177). The investigation of the effect of varying field strength was performed with the same samples on a second balance, an electromagnet being used. After the measurements, each sample container was cracked open, and the sample removed; the two parts of the container were then sealed together again and the magnetic effect on the empty container was measured.

In order to obtain the true paramagnetism of the quadrivalent plutonium ion the following diamagnetic corrections were applied: Th(IV), $31{\cdot}2 \times 10^{-6}$; Pu(IV), $40{\cdot}8 \times 10^{-6}$; O^{2-}, $11{\cdot}25 \times 10^{-6}$; F^-, $7{\cdot}25 \times 10^{-6}$. These values were calculated after the method of Angus (*Proc. Roy. Soc.*, **1932**, *A*, **136**, 569), the value for Pu(IV) being a mean of the $5f^4$ and $6d^4$ electron configurations.

The experimental results and the deduced magnetic susceptibilities of the Pu(IV) ion are given in Tables 1 and 2.

Table 1. PuF_4–ThF_4 *Solid solutions.**

Composition: Pu, %	T, ° K	$10^6 \times \chi_g$	$10^6 \times \chi_m$	$10^6 \times \chi_{Pu(IV)}$	Composition: Pu, %	T, ° K	$10^6 \times \chi_g$	$10^6 \times \chi_m$	$10^6 \times \chi_{Pu(IV)}$
100	90	9·482	2983	3053	52·0	90	7·249	2260	4470
	201	7·384	2326	2396		201	4·949	1543	3093
	301	5·589	1760	1830		301	3·512	1095	2232
	329	5·125	1614	1684		373	2·907	906·1	1868
	370	4·677	1473	1543		442·5	2·449	763·5	1593
	415·5	4·293	1353	1423					
	453	3·984	1255	1325					
77·8	90	9·168	2874	3781	34·0	90	5·745	1784	5434
	200	6·829	2141	2839		200	3·874	1203	3727
	300	4·878	1530	2053		300	2·527	784·6	2494
	329·5	4·543	1424	1917		334	2·306	755·5	2292
	378·5	4·049	1269	1718		362	2·036	672·0	2046
	412·5	3·718	1165	1584		418	1·783	593·1	1815
	441	3·494	1095	1494		442·5	1·489	555·7	1704
					3·6	300	0·142	43·8	2900
					2·0	300	0	0	3020

* χ_g = Gram susceptibility.
χ_m = Molar susceptibility.
$\chi_{Pu(IV)}$ = Susceptibility per g.-ion corrected for diamagnetism.

TABLE 2. PuO_2–ThO_2 *Solid solutions.*

Composition: Pu, %	T, ° K	$10^6 \times \chi_g$	$10^6 \times \chi_m$	$10^6 \times \chi_{Pu(IV)}$	Composition: Pu, %	T, ° K	$10^6 \times \chi_g$	$10^6 \times \chi_m$	$10^6 \times \chi_{Pu(IV)}$
100	90	4·859	1317	1381	35·3	90	2·475	659·8	2034
	200	3·258	883·0	946·3		200	1·548	412·5	1332
	300	2·693	730·2	793·5		300	1·294	344·8	1140
	333·5	2·577	698·4	761·7		328·5	1·158	308·5	1037
	367	2·543	689·0	752·3		371	1·117	397·6	1006
	406	2·426	657·3	720·6		411	1·062	283·0	965
	430	2·414	654·1	717·4		437	1·034	275·6	944
75	90	4·644	1251	1748	12·1	90	1·205	319·2	3090
	200·5	2·771	746·5	1076		201	0·552	146·2	1660
	300	2·168	584·0	859·8		299	0·344	91·1	1210
	334·5	2·055	553·7	819·5		334·5	0·303	80·2	1120
	372	1·942	523·0	778·5		375	0·260	69·0	1020
	411·5	1·852	499·0	746·5		414	0·230	60·9	955
	446·5	1·793	482·9	725·1		462	0·194	51·3	877
	521	1·754	472·3	710·1					
	592	1·675	451·2	682·7					
50·0	90	3·426	943·0	1949	8·82	300	0·280	74·1	1460
	199	2·034	571·1	1205	8·72	300	0·352	93·2	1580
	300	1·614	458·6	980	4·31	300	0·102	26·8	1880
	332	1·490	425·5	914	2·19	300	0·056	14·7	3140
	372	1·436	410·9	885					
	415	1·410	404·0	871					
	445	1·374	394·4	852					

DISCUSSION

The value of the dilution technique for the elucidation of the electron configuration of a paramagnetic ion lies in the fact that extrapolation to infinite dilution provides a value of the susceptibility more comparable with theoretically predicted values than that measured on the pure compounds, since the theoretical methods do not take account of any possible interaction between neighbouring ions.

The theoretical susceptibilities of the quadrivalent plutonium ion, various electron configurations being assumed and calculation being by Hund's method (*Z. Phys.*, 1925, **33**, 855), are in Table 3. Hund's method assumes that the multiplet separations are very wide compared to kT. Considering the lanthanides, Van Vleck has shown that the magnetic susceptibility may be affected by contributions from several low-lying energy states if the multiplet intervals are comparable to kT (" The Theory of Electric and Magnetic Susceptibilities," 1932, Chapter IX). His " intermediate " formula being used, and a $5f^4$ configuration being assumed with the electrons in L–S coupling, the theoretical susceptibility has been calculated at various temperatures (Table 4). Owing to the contributions from other low-lying states in addition to the predicted ground state, the theoretical susceptibility at 300° K is somewhat higher in Table 4 than in Table 3.

TABLE 3. *Theoretical magnetic susceptibilities at* 300° K (*Hund ; L–S coupling.*)

Configuration	Conditions	$10^6 \times \chi$
$5f^4$	No interaction	3,010 [a]
$5f^3 6d^1$	No orbital contribution from the $6d$ electrons	3,010
$5f^2 6d^2$		1,250
$5f^1 6d^3$		0
$6d^4$	" Spin-only " value	10,500

[a] The j–j value is about 6100×10^{-6}.

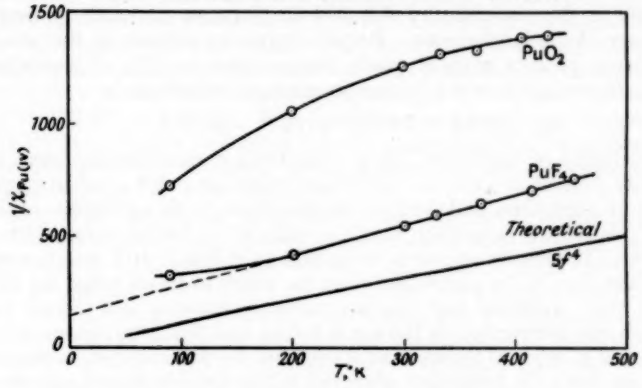
TABLE 4. *Theoretical susceptibility of* Pu(IV) *with* $5f^4$ *configuration* (*Van Vleck*).

T, ° K	50	100	200	300	400	500	600
$10^6 \chi$	17,840	9035	4632	3165	2434	2003	1724

The value of the screening constant used in the calculation was 58, this having been shown by Dawson, Mandleberg, and Davies (*J.*, 1951, 2047) to be the most probable value for plutonium. The screening constant does not have such a marked effect on the theoretical susceptibility for the Pu(IV) ion as for the Pu(III) ion. Use of the value 57 instead of 58 gives a susceptibility less than 1% lower.

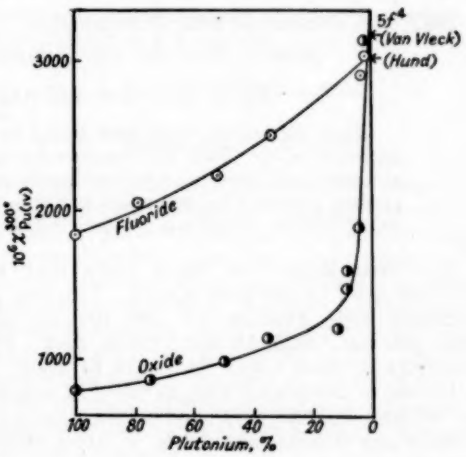
Plutonium Tetrafluoride.—The observed value of the magnetic susceptibility at 300° K (1830×10^{-6}) is somewhat lower than the value (1980×10^{-6}) quoted by Elliott and Lewis (*loc. cit.*). The variation of reciprocal susceptibility of the pure substance with temperature is shown in Fig. 1 and agrees with Elliott and Lewis's assertion that there is an upward

FIG. 1. *Susceptibility–temperature behaviour of* Pu(IV).



curvature away from the straight line of the Curie–Weiss law. This occurs only below 200° K, however; above that temperature the Curie–Weiss law is a good approximation to the behaviour of the susceptibility. The theoretical curve derived from Table 4, also shown in Fig. 1, does not quite follow the Curie–Weiss law, there being a slight downward curvature scarcely visible on the reduced scale. Dilution in solid solution does not have any effect on the deviation of the experimental susceptibility at 90° K, at least down to 34% of plutonium which was the most dilute solution investigated at this temperature.

FIG. 2. PuO_2–ThO_2 *and* PuF_4–ThF_4 *solid solutions.*



The variation of susceptibility at 300° K with plutonium concentration is shown in Fig. 2. Extrapolation to infinite dilution gives a susceptibility of about 3020×10^{-6}. This value is in reasonable agreement with that predicted for a $5f^4$ electron configuration with L–S coupling (see Tables 3 and 4). The theoretical value for a $5f^3 . 6d^1$ configuration is the same as that for $5f^4$ (Hund values) but the tetrafluoride solid solutions show no evidence of the exchange forces which would be expected from the presence of *d*-shell electrons.

Direct comparison with the lanthanide series is not possible since the corresponding ion with four electrons would be Pm(III) on which no results are available. However, the tervalent praseodymium ion in the octahydr: ed sulphate shows an upward curvature away from the Curie–Weiss law, similar to that observed above, and Penney and Schlapp (*Phys. Review*, 1932, **41**, 194) have explained this by a consideration of the redistribution of the magnetic levels due to the effect of the crystal electric field. It is possible that the similar effect in plutonium tetrafluoride may arise in the same way.

Plutonium Dioxide.—The variation of reciprocal susceptibility with temperature of the Pu(IV) ion in the oxide lattice is quite different from that in the fluoride (Fig. 1). It is fairly closely represented over the investigated temperature range by the expression :

$$(\chi - 542{\cdot}9 \times 10^{-6})(T + 0{\cdot}14) = 0{\cdot}0756$$

This is similar to the formula used by Cabrera and Duperier (*Compt. rend.*, 1927, **185**, 414; 1929, **188**, 1640) for the susceptibility of ions of the platinum- and palladium-group elements and also of some of the lanthanides. Despite increasing dilution in thorium dioxide, this type of behaviour persists without much change down to 12% of plutonium (the most dilute solution investigated over a temperature range), which gives

$$(\chi - 276{\cdot}1 \times 10^{-6})(T + 13{\cdot}1) = 0{\cdot}2901$$

The susceptibility of the Pu(IV) ion in pure PuO_2 is considerably lower than in PuF_4 and is very low compared with the theoretical value for a $5f^4$ configuration. However, between 10% of plutonium and infinite dilution there is an extremely rapid rise in the susceptibility; in fact, it is so steep that it is difficult to fix the value of the intercept at infinite dilution. It does not appear to be as high as $10{,}500 \times 10^{-6}$, which would indicate a $6d^4$ configuration, but to be somewhere near the value to be expected for $5f^4$ or $5f^3 . 6d^1$ (Fig. 2). The above evidence might be interpreted as showing that there is a considerable amount of exchange interaction in the oxide lattice and that this persists so long as more than some critical number of lattice sites is occupied by paramagnetic plutonium ions. It is quite different from the behaviour observed in the fluoride lattice and may favour the supposition of a $5f^3 . 6d^1$ electron configuration rather than $5f^4$.

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ATOMIC ENERGY RESEARCH ESTABLISHMENT,
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347. *Nitramines and Nitramides. Part III.* The Formation of Nitric Acid by the Action of Sulphuric Acid.*

By C. HOLSTEAD and ALEX. H. LAMBERTON.

Many nitramides have been found to give nitric acid on dissolution in sulphuric acid. With the noteworthy exception of cyclonite, nitramines give little, and often no, nitric acid under similar conditions. A condensation product has been isolated which indicates that nitramine, in association with formaldehyde, can play a synthetic role in concentrated sulphuric acid.

IT has been known for many years that some *N*-nitro-compounds could act, in sulphuric acid, as nitrating agents. This has been demonstrated by the use of nitrourethane (Thiele, *Annalen*, 1897, **296**, 108), nitroguanidine (Davis and Abrams, *Proc. Amer. Acad. Arts Sci.*, 1926, **61**, 437; *Chem. Zentr.*, 1927, I, 2295), and nitrobiuret (Davis and Blanchard, *J. Amer. Chem. Soc.*, 1929, **51**, 1801). Denitration is also known to be possible in the case of compounds such as tetryl (Romburgh, *Rec. Trav. chim.*, 1886, **5**, 240; Jones and Willson, *J.*, 1930, 2277), and occurs, though very possibly without the actual liberation of nitric acid (Hughes and Jones, *J.*, 1950, 2678), in the Bamberger–Orton conversion of aromatic nitramines into *C*-nitro-anilines.

Little stress has hitherto been laid on these observations, and the reaction appears to be more general than had been supposed. We have added, under standard conditions, various *N*-nitro-compounds to acetanilide (1 molecule for each nitro-group potentially available) dissolved in the sulphuric acid, and have used the formation of *p*-nitroacetanilide as a measure of the nitric acid produced.

The compounds examined may, for convenience in discussion, be divided into three

* *J.*, 1949, 1883, and 1951, 1282, are regarded as Parts I and II of this series.

groups. In the first group (Experimental, Table 1) we place the nitramides, both primary and secondary, and also the nitroguanidines. It is true that the zwitterionic nitroguanidines are not themselves nitramides, but we are here dealing with their salts [*e.g.*, $NO_2{\cdot}NH{\cdot}C(NH_2)_2^+$], and the amidinium portion $-C(NH_2)_2^+$ may be regarded as acylic in character. In the second group (Experimental, Table 3) we consider some simple secondary nitramines. They have been found, in many cases, to be stable under conditions which usually bring about the liberation of nitric acid from compounds in Group I; and, even under more drastic treatment, little, if any, nitric acid is formed. The third group (Experimental, Table 4) consists of derivatives of methylenediamine, and might be further sub-divided into the aminomethylnitramines ($R_2N{\cdot}CH_2{\cdot}NR'{\cdot}NO_2$) and the methylenepolynitramines ($NO_2{\cdot}NR{\cdot}CH_2{\cdot}NR{\cdot}NO_2$). The common feature of the compounds in the third group is that methylene fragments may become available for synthetic purposes. Nitric acid was also produced, though only in significant amounts when stronger sulphuric acid (99·7% in place of 95·2%, w/w) was used.

It can be seen from Table 1 (p. 1889) that nitroguanidine (2), ethylnitroguanidine (3), nitrourea (5), nitrourethane (6), and a range of secondary nitramides which can be regarded as structurally related to nitrourethane [7—12; all contain $-N(NO_2){\cdot}CO{\cdot}O^-$] furnished nitric acid readily, and often provided a better yield of *p*-nitroacetanilide than potassium nitrate itself. The isolation of guanidine, urethane, and *N*-alkylurethanes suggests a simple denitration: it may be that the nitration process is reversible, though our qualitative evidence is not a strict proof. R. J. J. Simkins and G. Williams (personal communication) have shown, by quantitative measurements, that the conversion of the guanidinium ion into the nitroguanidinium ion is reversible. The yield of *p*-nitroacetanilide from the carbonic acid derivative, ethylenedinitrourea (tetrahydro-2-keto-1 : 3-dinitroglyoxaline) (13), showed that both nitro-groups were available. The acetyl compound examined (17) did not provide nitric acid, and was shown to give acetic acid on treatment with sulphuric acid alone.

The *N*-nitrosulphonamides (14, 15, and 16) gave some nitric acid, though the yield from (16) was small, and *p*-nitroacetanilide could not in this case be isolated by our normal technique. The formation of toluene-*p*-sulphonic acid suggested competitive modes of decomposition. If the overall reaction is formulated as a hydrolysis, these are

$$Me{\cdot}C_6H_4{\cdot}SO_2{\cdot}NR{\cdot}NO_2 + H_2O \xrightarrow{A} Me{\cdot}C_6H_4{\cdot}SO_2{\cdot}NHR + HNO_2$$
$$Me{\cdot}C_6H_4{\cdot}SO_2{\cdot}NR{\cdot}NO_2 + H_2O \xrightarrow{B} Me{\cdot}C_6H_4{\cdot}SO_3H + R{\cdot}NH{\cdot}NO_2$$

and it was found that the nitric acid formed by route A converted a considerable proportion of the sulphonic acid (route B) into *o*-nitrotoluene-*p*-sulphonic acid. Changing the strength of sulphuric acid from 95% to 100% (w/w) had very little influence on the outcome, though the change possibly favoured route A. It seemed unlikely, since we found no sign of the production of *o*-nitrotoluene-*p*-sulphonamides, that the nitric acid formed by partial decomposition converted any of the residual nitramide into an *N*-nitro-*o*-nitrotoluene-*p*-sulphonamide. Treatment of the *N*-nitrosulphonamides with sulphuric acid alone (Table 2) confirmed these results. Estimation of the total yield of the various products (p. 1891) suggested that the addition of acetanilide had no influence upon the routes of decomposition when (15) a sufficiency of the nitratable toluene-*p*-sulphonic acid was in any case formed: when this was not so (14), the addition of acetanilide slightly favoured the (reversible) route *A* through the removal of nitric acid.

The simple secondary nitramines (Table 3) did not, with the exception of di*cyclo*hexylnitramine (21), give any *p*-nitroacetanilide. In 95% sulphuric acid this was in part due to their stability (19*a*, 20*a*); but, even under conditions drastic enough to decompose all (or most) of the nitramine, no nitroacetanilide was obtained. The recovery of part of the acetanilide showed that, if it had been formed, nitric acid would have had the opportunity of nitrating the anilide: *p*-nitroacetanilide was found, in separate experiments, to be unaffected by sulphuric acid under the conditions used. We conclude that significant quantities of nitric acid cannot be formed by the decomposition of these nitramines.

Franchimont and his school made several vague references (*e.g.*, *Rec. Trav. chim.*, 1898, **17**, 287) to the action of sulphuric acid on secondary nitramines; and Backer (*Ahrens Sammlung*, 1912, **18**, 359) suggested the formation of either a hydroxylamine or a Schiff's base as intermediates in the ultimate production of an amine and a carbonyl compound :

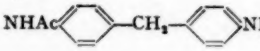
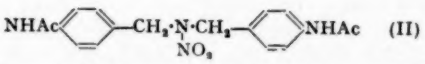
$$R{\cdot}N(NO_3){\cdot}CHR'R'' + H_2SO_4 \rightarrow \begin{cases} (NO)(HSO_4) + R{\cdot}N(OH){\cdot}CHR'R'' \\ HNO_2 + R{\cdot}N{:}CR'R'' \end{cases} \xrightarrow{(+H_2O)} R{\cdot}NH_2 + R'R''CO$$

We have examined the products which resulted from the action of sulphuric acid alone (95·2% w/w) on di*cyclo*hexylnitramine and on dimethylnitramine. In the first case di*cyclo*hexylnitrosamine was precipitated on dilution with water : from the filtrate, which contained nitrous acid, *cyclo*hexylamine and *cyclo*hexanone were isolated as, respectively, the toluene-*p*-sulphonamide and the 2 : 4-dinitrophenylhydrazone. In all, 44% of the initial nitramine could be accounted for. The more stable dimethylnitramine has similarly been shown to yield at least some nitrous acid, formaldehyde, and methylamine. It appears that the suggestion of the early workers regarding the final products is correct, but we do not feel able, at present, to comment on the course of the reaction. The formation of the nitrosamine is incidental—since this product was found to be unaltered by further treatment with sulphuric acid—and is not unprecedented (Reverdin, *Chem. Zentr.*, 1910, I, 1020; 1911, I, 548; 1912, II, 110).

It was suggested to us, very pertinently, by Dr. J. P. Picard that denitration might occur only in those cases where the *N*-nitro-compound could be formed by direct nitration without the use of a chloride catalyst (Wright *et al.*, *Canad. J. Res.*, 1948, **26**, *B*, 89, 114). For this reason we examined two cyanonitramines (22 and 23) which can be prepared by the direct nitration of the parent (weakly basic) secondary amines. There was, however, no sign of denitration : instead, these cyanides were converted into the corresponding diamides.

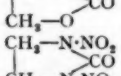
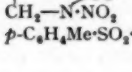
Among the compounds listed in Table 4 only cyclonite (31) gave more than traces of *p*-nitroacetanilide on treatment with acetanilide in 95·2% sulphuric acid. The denitration reaction was obviously favoured by an increase in the sulphuric acid concentration : this effect was shown both in the case of aminomethylnitramines (28, 30) and cyclic polynitramines (31, 32, 33). The efficiency of cyclonite as a nitrating agent was more than twice that of any of the other compounds examined, and compares, at least in 99·7% acid, not too unfavourably with potassium nitrate itself. In all the compounds of this group gas was evolved on dissolution. This is known, at least in the case of cyclonite (E. Roberts, private communication), to be nitrous oxide; and a further portion of the initial nitrogen of cyclonite is converted into ammonium ions.

Condensation products were formed in most cases from acetanilide and fragments of the added nitramines. One such was di-*p*-acetamidophenylmethane (I) which is known (Ralston and McCorkle, *J. Amer. Chem. Soc.*, 1939, **61**, 1604) and results also from the addition of paraformaldehyde to acetanilide in sulphuric acid. The production of di-*p*-acetamidobenzylnitramine (II) indicates that nitramine (presumably closely associated with, and stabilised by, " formaldehyde ") can play a synthetic role in media as destructive as anhydrous sulphuric acid. The combined yield of compounds (I) and (II) in a crude condition was often considerable, but separation and purification was difficult. The best source of (II) was the linear polymethylenenitramine " B.S.X. " (29) and the structure of (II) has been proved by (*a*) hydrolysis to the nitramino-diamine (II; H in place of Ac), (*b*) reduction by zinc and acetic acid to (probably) the diacetyl-triamine (II; H in place of NO_2), and (*c*) reduction by tin and hydrochloric acid to the triamine (II; H in place of Ac and of NO_2).

(I)  (II) 

We have examined (since this nitramine is probably formed by sulphuric acid from the nitramides 16 or 17, and may also result from the fragmentation of 27, 30, or 32) the behaviour of ethylenedinitramine under our standard experimental conditions.

TABLE 1. *Action of nitroguanidines and of nitramides on acetanilide in sulphuric acid of (a) 95·2%, and (b) 99·7%, w/w.*

Ref. no.	*N*-Nitro-compound	Yield (%) of $NO_2{\cdot}C_6H_4{\cdot}NHAc$	Other products isolated
1*a*	KNO_3 (Standard)	72	—
1*b*	,, ,,	44—55	—
2*a*	$NH_2{\cdot}C(NH){\cdot}NH{\cdot}NO_2$	73	Guanidine (50%; note 1)
3*a*	$Et{\cdot}NH{\cdot}C(NH){\cdot}NH{\cdot}NO_2$	76	—
3*b*	,,	44—51	—
4*a*	$NH_2{\cdot}C(NH){\cdot}NH{\cdot}CO{\cdot}NH{\cdot}NO_2$	66	—
4*b*	,,	41—53	—
5*a*	$NH_2{\cdot}CO{\cdot}NH{\cdot}NO_2$	60	—
5*b*	,,	41—52	—
6*a*	$EtO_2C{\cdot}NH{\cdot}NO_2$	81	Urethane (33%; m. p. 45—48°; note 2)
6*b*	,,	43—55	—
7*a*	$EtO_2C{\cdot}NMe{\cdot}NO_2$	79	$EtO_2C{\cdot}NHMe$ (39%; b. p. 67°/17 mm.; note 2)
8*a*	$EtO_2C{\cdot}NPr^i{\cdot}NO_2$	72	$EtO_2C{\cdot}NHPr^i$ (76%; b. p. 71°/12 mm.; note 2)
9*a*	$EtO_2C{\cdot}N(NO_2){\cdot}CH_2{\cdot}CO_2Et$	78	—
10*a*	$EtO_2C{\cdot}N(NO_2){\cdot}[CH_2]_3{\cdot}N(NO_2){\cdot}CO_2Et$	70	—
10*b*	,,	41—55	—
11*a*	$MeO_2C{\cdot}N(NO_2){\cdot}[CH_2]_3{\cdot}N(NO_2){\cdot}CO_2Me$	78	—
12*a*		79	—
13*a*		76	—
14*a*	$p\text{-}C_6H_4Me{\cdot}SO_2{\cdot}NH{\cdot}NO_2$	39	Ph·NHAc, $C_6H_4Me{\cdot}SO_2{\cdot}NH_2$ (33%; note 3), $C_6H_4Me{\cdot}SO_3H$ (30%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (1%; note 4)
14*b*	,,	42	$C_6H_4Me{\cdot}SO_2{\cdot}NH_2$ (35%; note 3), $C_6H_4Me{\cdot}SO_3H$ (15%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (9%; note 4)
15*a*	$p\text{-}C_6H_4Me{\cdot}SO_2{\cdot}NMe{\cdot}NO_2$	15	Ph·NHAc, $C_6H_4Me{\cdot}SO_2{\cdot}NHMe$ (19%; note 3), $C_6H_4Me{\cdot}SO_3H$ (50%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (5%; note 4)
15*b*	,,	18	$C_6H_4Me{\cdot}SO_2{\cdot}NHMe$ (24%; note 3), $C_6H_4Me{\cdot}SO_3H$ (34%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (8%; note 4)
16*a*	$[{\cdot}CH_2{\cdot}N(NO_2){\cdot}SO_2{\cdot}C_6H_4Me]_2$	1 (note 5)	Ph·NHAc, $C_6H_4Me{\cdot}SO_3H$ (70%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (2%; note 4)
16*b*	,,	4 (note 5)	$C_6H_4Me{\cdot}SO_3H$ (61%; note 4), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (3%; note 4)
17*a*	$[{\cdot}CH_2{\cdot}N(NO_2){\cdot}COMe]_2$	Nil (note 5)	Ph·NHAc
17*b*	,,	Nil (note 5)	AcOH (71%; note 6)

Notes: (1) The initial filtrate was basified with barium hydroxide, the barium sulphate removed, and the excess of barium hydroxide precipitated as the carbonate by the passage of carbon dioxide. After filtration, nitric acid (2·5 ml.; 70%) was added, and the liquid evaporated to 10 ml. Cooling yielded guanidine as the nitrate, identified by m. p. and reconversion into nitroguanidine. (2) The initial filtrate was extracted with ether; when dried and distilled *in vacuo* the extract yielded a urethane, which was identified by m. p. or b. p., and by alkaline hydrolysis to yield a volatile base (ammonia, methylamine, or *iso*propylamine) which was converted into the corresponding toluene-*p*-sulphonamide. (3) The sulphonamides, which formed part of the initial precipitate, were separated by dissolution in aqueous sodium hydroxide, and were precipitated in a pure state on acidification. (4) The initial filtrate was treated with an aqueous solution of *S*-benzylthiuronium hydrochloride to precipitate the *S*-benzylthiuronium salts of toluene-*p*-sulphonic acid and *o*-nitrotoluene-*p*-sulphonic acid. The collected mixture of salts was analysed by (*a*) comparison of its m. p. with the m. p. diagram of mixtures of authentic materials, and (*b*) elemental (carbon) analysis. The mean value has been used in the calculation of yields. The following tabulation gives, successively, the reference number, the number of parts of the nitrated salt in 100 parts of the mixture as determined by methods (*a*) and (*b*), and the C, H values found for the mixture: 14*a*; 5, 4; C, 53·0; H, 5·8%. 14*b*; 39, 38; C, 50·9; H, 5·3%. 15*a*; 8, 9; C, 52·7; H, 5·6%. 15*b*; 22, 19; C, 52·2; H, 5·4%. 16*a*; 3, 3; C, 53·1; H, 5·6%. 16*b*; 6, 3; C, 53·1; H, 5·6% (Calc., for the salt of toluene-*p*-sulphonic acid, $C_{15}H_{18}O_3N_2S_2$; C, 53·3; H, 5·3%. Calc., for the salt of *o*-nitrotoluene-*p*-sulphonic acid, $C_{15}H_{17}O_5N_3S_2$: C, 47·0; H, 4·4%.) (5) *p*-Nitroacetanilide could not be isolated by the usual crystallisation from alcohol. Compound (16) gave the yields quoted on crystallisation from water, but no yield was thus obtained from (17). (6) After neutralisation with barium hydroxide acetic acid was precipitated from the initial filtrate as the *S*-benzylthiuronium salt. A comparable yield was obtained by treatment of the nitramide with sulphuric acid alone; hence the acetic acid cannot have come, in any quantity, from the acetanilide.

As was expected, from the known instability of primary nitramines towards acids, dissolution occurred with the immediate evolution of, presumably, nitrous oxide, and no *p*-nitroacetanilide was formed. The use of ethylenedinitramine provided an additional example of the behaviour, towards 95·2% w/w sulphuric acid, of a series of compounds of the general formula $NO_2{\cdot}NR{\cdot}CH_2{\cdot}CH_2{\cdot}NR{\cdot}NO_2$. These, if tabulated in the probable order of increasing acidity of ROH, are R = Me (19), H, $CMe_2{\cdot}CN$ (23), CO_2Et (10), $CO{\cdot}CH_3$ (17), and $SO_2{\cdot}C_6H_4Me$ (16). Of these only the urethane (10) and the sulphonamide (16) yielded nitric acid.

Experimental

Action of Nitramines and Nitramides on Acetanilide in Sulphuric Acid.—The *N*-nitro-compound (0·02 g.-equiv. of NO_2) was added, with stirring, in 20 minutes at 25°, to acetanilide (0·02 mole) freshly dissolved in sulphuric acid [20 ml. of (*a*) 95·2% or (*b*) 99·7%, w/w]. After a further 20 minutes at 25° the mixture was poured into ice and water (150 ml.). The precipitate was collected and crystallised from alcohol (50 ml.), for isolation of *p*-nitroacetanilide : a second crop was obtained by evaporation of the alcoholic mother-liquor to 10 ml. Yields quoted, in the *a* series, are the sum of these crops : m. p. >208°. In the *b* series the second crop was often impure, and the yields are then quoted as a range : *e.g.*, 44—55% indicates 44% of m. p. >208° and a second crop of 11%, m. p. >190° but <208°. Potassium nitrate was used, under identical conditions, as a standard for comparison (see Table 1).

Table 2. *Action of sulphuric acid on nitramides.*

Ref. no.	*N*-Nitro-compound	Concn. of H_2SO_4 (w/w)	Products isolated
14*c*	*p*-$C_6H_4Me{\cdot}SO_2{\cdot}NH{\cdot}NO_2$	95·2%	$C_6H_4Me{\cdot}SO_2{\cdot}NH_2$ (37% of m. p. 136°), $C_6H_4Me{\cdot}SO_3H$ (2%; note 1), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (41%; note 1)
14*d*	,,	99·7%	$C_6H_4Me{\cdot}SO_2{\cdot}NH_2$ (36% of m. p. 135°), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (39%; note 1)
15*c*	*p*-$C_6H_4Me{\cdot}SO_2{\cdot}NMe{\cdot}NO_2$	95·2%	$C_6H_4Me{\cdot}SO_2{\cdot}NHMe$ (23% of m. p. 76°), $C_6H_4Me{\cdot}SO_3H$ (31%; note 1), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (21%; note 1)
15*d*	,,	99·7%	$C_6H_4Me{\cdot}SO_2{\cdot}NHMe$ (28% of m. p. 76°), $C_6H_4Me{\cdot}SO_3H$ (14%; note 1), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (31%; note 1)
16*c*	$[{\cdot}CH_2{\cdot}N(NO_2){\cdot}SO_2{\cdot}C_6H_4Me]_2$	95·2%	$C_6H_4Me{\cdot}SO_3H$ (62%; note 1), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (9%; note 1)
16*d*	,,	99·7%	$C_6H_4Me{\cdot}SO_3H$ (58%; note 1), and $C_6H_3Me(NO_2){\cdot}SO_3H$ (20%; note 1)
17*c*	$[{\cdot}CH_2{\cdot}N(NO_2){\cdot}COMe]_2$	95·2%	AcOH (61%; note 2)

Notes: (1) The mixed *S*-benzylthiuronium salts of toluene-*p*-sulphonic acid and *o*-nitrotoluene-*p*-sulphonic acid were analysed as described in note 3 to Table 1 ; the results, reported in similar style, were : 14*c*; 98, 91; C, 47·6; H, 4·3%. 14*d*; 100, 100; C, 47·0; H, 4·5%. 15*c*; 48, 40; C, 50·8; H, 4·9%. 15*d*; 69, 76; C, 48·5; H, 4·9%. 16*c*; 15, 10; C, 52·7; H, 5·5%. 16*d*; 25, 31; C, 51·3; H, 5·4%. For calc. and required values, see note 4 to Table 1. (2) No precipitate was obtained on dilution of the solution of (17) in sulphuric acid with water, and extraction with methylene dichloride yielded no unchanged nitramide. After neutralisation with barium hydroxide, acetic acid was isolated as the *S*-benzylthiuronium salt of m. p. 150°.

Unchanged acetanilide was recovered from the majority of mixtures in which nitration to *p*-nitroacetanilide had not occurred. In the *a* series the acetanilide, if present in sufficient quantity, was precipitated on dilution with water, whilst in the *b* series it was necessary to extract it with ether. The isolation of acetanilide, when performed, is indicated in the tables, but the lack of indication for a particular experiment does not imply that residual acetanilide was proved to be absent.

Further details are given as notes after the individual tables. In these the expressions " initial ppt. " and " initial filtrate " refer to the precipitate, and the filtrate therefrom, which were obtained on pouring the sulphuric acid mixture into ice and water (150 ml.).

All products (apart from those which were analysed) were identified by m. p. and mixed m. p. with authentic materials. In some cases half-scale experiments were made, without any other alteration in procedure.

Stability of p-*Nitroacetanilide in Sulphuric Acid.*—*p*-Nitroacetanilide (3 g.) was added in

20 minutes at 25° to sulphuric acid (20 ml.). After a further 20 minutes at 25°, the residual *p*-nitroacetanilide was recovered by our standard procedure: recovery 86% and 67—79%, from 95·2% w/w and 99·7% w/w acid, respectively. After 16 hours at 25° in the 99·7% w/w acid, the recovery was 62—76%.

Treatment of Some Nitramides with Sulphuric Acid Alone.—The nitramides were treated with sulphuric acid under our standard conditions, but in the absence of acetanilide. Sulphonamides, when formed, were precipitated in a pure condition on dilution with water. Sulphonic acids, and acetic acid, were isolated as *S*-benzylthiuronium salts. Details are given in Table 2.

Balance-sheet of Materials in Experiments with N-Nitrosulphonamides.—Isolation of the products of decomposition could not be quantitative, since the sulphonamides and the *S*-benzylthiuronium salts are slightly water-soluble. We found, as a result of trial precipitations under our standard conditions, that the loss of toluene-*p*-sulphonamide was approximately 25% of the theoretically possible yield in experiments **14***a* and **14***b* (which involve two precipitations) and 16% in experiments **14***c* and **14***d*. The loss, for the less soluble *N*-methyltoluene-*p*-sulphonamide, was 11% in experiments **15***a* and **15***b*, and 7% in experiments **15***c* and **15***d*. Similarly, the probable losses of the *S*-benzylthiuronium salts of toluene-*p*-sulphonic acid and *o*-nitrotoluene-*p*-sulphonic acid were 8 and 6% respectively. By adding these figures to the percentage yields isolated (as quoted in Tables 1 and 2) we estimated the total yield of the various products. In experiments **14***a* to **14***d*, and **15***a* to **15***d*, this total of sulphonamide *plus* sulphonic acids was 100 ± 10% (average 99%), whilst the difference between the sulphonamide and the total of nitrated products (*o*-nitrotoluene-*p*-sulphonic acid and, if relevant, *crude* *p*-nitroacetanilide) was never more than 8% (average, sulphonamide 3% > total of nitrated materials). These figures enable us to say, with some confidence, that the routes A and B (p. 1887) are the only significant modes of decomposition.

With compound (**16**) the balance was less exact. We could account for about 85% of the initial material, and, in addition, a little ill-defined sulphonamide-like material could be isolated but not characterised. This was hardly surprising, since the total of nitric acid was low, and both nitramide groups must independently give rise to nitric acid if the pure disulphonamide is to be formed.

Separation of the S-*Benzylthiuronium Salts of Toluene*-p-*sulphonic Acid and* o-*Nitrotoluene*-p-*sulphonic Acid.*—The mixture of salts (*e.g.*, from experiment **15***c*) (0·4 g. of m. p. 161—164°) was decomposed by dissolution in 2N-sodium hydroxide (4 ml.). After a few minutes the solution was acidified with 2N-hydrochloric acid (5 ml.) and the liberated toluene-ω-thiol volatilised by boiling to a volume of 3 ml. Addition of barium chloride (4 ml. of M/4) to the cooled concentrate precipitated barium *o*-nitrotoluene-*p*-sulphonate, which was collected, dissolved in hot water, and reconverted, by the addition of *S*-benzylthiuronium hydrochloride and cooling, into the pure S-*benzylthiuronium* salt [0·06 g. of m. p. 163—164°, identical with material produced in experiment **14***d* (*q.v.* for analysis) or prepared from authentic *o*-nitrotoluene-*p*-sulphonic acid]. Treatment of the mother-liquor from the collection of barium *o*-nitrotoluene-*p*-sulphonate with *S*-benzylthiuronium hydrochloride gave a crude salt of toluene-*p*-sulphonic acid (0·06 g. of m. p. 175—177°; the pure salt has m. p. 181°) which still contained about 12% of the nitrated acid.

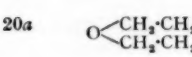
Treatment of Some Secondary Nitramines with Sulphuric Acid Alone.—(*a*) Di*cyclo*hexylnitramine was treated with sulphuric acid (95·2% w/w) under our standard conditions, but in the absence of acetanilide. The precipitate obtained on dilution was collected and crystallised from alcohol, to yield di*cyclo*hexylnitrosamine (13%; m. p. 102°). Half of the aqueous filtrate was basified with sodium hydroxide, and steam-distilled; from the distillate *cyclo*hexylamine was isolated in 10% yield as *N*-*cyclo*hexyltoluene-*p*-sulphonamide (m. p. 86°, as given by Hall and Turner, *J.*, 1945, 696). From the remaining half, *cyclo*hexanone was isolated (in 31% yield on basis 1 mole of nitramine ⟶ 1 mole of *cyclo*hexanone) as the 2 : 4-dinitrophenylhydrazone, m. p. 157°. *cyclo*Hexanone was characterised, additionally, by formation of the semicarbazone (m. p. 166°). In this, as in experiment **21***a*, the di*cyclo*hexylnitrosamine was of lower m. p. than the material (105°) obtained from experiment **21***b*, or synthetically. We believe that the impurity was unchanged di*cyclo*hexylnitramine. Re-treatment with sulphuric acid gave pure di*cyclo*hexylnitrosamine and showed, since the recovery was nearly quantitative, that the nitrosamine cannot be an intermediate in the formation of *cyclo*hexylamine and of *cyclo*hexanone.

(*b*) Similar treatment of dimethylnitramine gave dimethylamine (19%; determined by distillation into standard hydrochloric acid), identified by formation of *N*-methyltoluene-*p*-sulphonamide (m. p. 77°), and the 2 : 4-dinitrophenylhydrazone of formaldehyde (18%; m. p. 162°). In addition, 8% of the original nitramine could be recovered.

(*c*) Nitromorpholine was treated under our standard conditions with sulphuric acid alone (95·2%, w/w), and was recovered (79%) by extraction of the diluted aqueous acid with chloroform, and vacuum-distillation.

In all cases (*a*, *b*, and *c*) the diluted aqueous acid was found to contain nitrous acid by the sulphanilic acid–α-naphthylamine colour test.

TABLE 3. *Action of simple secondary nitramides on acetanilide in sulphuric acid of* (*a*) 95·2% *and* (*b*) 99·7%, *w/w.*

Ref. no.	*N*-Nitro-compound	Products isolated, and remarks
18*a*	$Me_2N{\cdot}NO_2$	Ph·NHAc, and initial nitramine (28%; note 1)
18*b* (1)	,,	,, (20%; note 1)
18*b* (2)	,,	Kept, after addition, for 15 hours at 25°; no nitramine recovered
19*a* (1)	$NMe(NO_2){\cdot}CH_2{\cdot}CH_2{\cdot}NMe(NO_2)$	Ph·NHAc, and initial nitramine (80%; note 2)
19*a* (2)	,,	Kept, after addition, for 1½ hours at 50°: Ph·NHAc, and initial nitramine (44%; note 3)
19*a* (3)	,,	Kept, after addition, for 70 hours at 25°: initial nitramine (38%; note 3)
19*b*	,,	Kept, after addition, for 15 hours at 25°; initial nitramine (39%; note 3)
20*a*		Ph·NHAc; initial nitramine presumably unchanged (see action of sulphuric acid alone), but not isolated from filtrate
20*b* (1)	,,	Initial nitramine (44%; note 4)
20*b* (2)	,,	Kept, after addition, for 15 hours at 25°; no nitramine recovered
21*a*	$(C_6H_{11})_2N{\cdot}NO_2$	*p*-Nitroacetanilide (7%), and di*cyclo*hexylnitrosamine (10%; note 5)
21*b*	,,	*p*-Nitroacetanilide (11%), and di*cyclo*hexylnitrosamine (13%; note 5)
22*a*	$CN{\cdot}CH_2{\cdot}N(NO_2){\cdot}CH_2{\cdot}CN$	Ph·NHAc, and amide (14%; note 6)
23*a*	$[{\cdot}CH_2{\cdot}N(NO_2){\cdot}CMe_2{\cdot}CN]_2$	Ph·NHAc, and amide (66%; note 7)
24*b*	$(p\text{-}NHAc{\cdot}C_6H_4{\cdot}CH_2)_2N{\cdot}NO_2$	Initial nitramine (57%; note 3)

Notes: (1) Dimethylnitramine was extracted from the initial filtrate with ether, and separated from acetanilide by sublimation. (2) Acetanilide was removed from the initial ppt. by cold alcohol leaving a residue of pure *NN'*-dimethylethylenedinitramine. (3) The initial ppt. consisted solely of unchanged nitramine. (4) No initial ppt. was obtained; the solution was extracted with chloroform, and pure nitromorpholine isolated by distillation *in vacuo*. (5) The initial ppt. was triturated with cold ether, and the insoluble *p*-nitroacetanilide worked up in the usual manner. The ethereal solution was evaporated, and the residue crystallised from aqueous alcohol, to yield di*cyclo*hexylnitrosamine. (6) After 3 days the initial filtrate deposited the diamide (14%; m. p. 223°), which crystallised from water in shining plates, m. p. 224° (decomp.) (Found: C, 27·6; H, 4·3; N, 31·5. Calc. for $C_4H_8O_4N_4$: C, 27·3; H, 4·4; N, 31·7%). Franchimont and Dubsky (*Rec. Trav. chim.*, 1916, **36**, 104) gave m. p. 218° (decomp.) for a crude specimen. (7) Acetanilide was removed from the initial ppt. by trituration with cold alcohol. The insoluble *NN'-di-(2-carbamylprop-2-yl)ethylenebisnitramine* (66%; m. p. 274°, decomp.) crystallised from water in prisms; m. p. 278° (decomp.) (Found: C, 37·8; H, 6·0; N, 25·8. $C_{10}H_{20}O_6N_6$ requires C, 37·5; H, 6·3; N, 26·2%).

Di-p-*acetamidophenylmethane* (I).—Acetanilide (2·7 g.) was dissolved in concentrated sulphuric acid (20 ml.), and paraformaldehyde (0·1 g.) added portionwise at 25° in 20 minutes. After a further 20 minutes the mixture was poured into ice and water (150 ml.), and the resultant precipitate crystallised several times from alcohol, to yield di-*p*-acetamidophenylmethane (0·1 g.), m. p. 233° (Found: C, 72·2; H, 6·4; N, 9·8. Calc. for $C_{17}H_{18}O_2N_2$: C, 72·3; H, 6·4; N, 9·9%). Authentic material prepared from di-*p*-aminophenylmethane and acetic anhydride. M. p.s ranging from 227° to 236° have been reported (Ralston and McCorkle, *loc. cit.*).

Di-p-*acetamidobenzylnitramine* (II).—1 : 7-Diacetoxy-2 : 4 : 6-trinitro-2 : 4 : 6-triazaheptane ("B.S.X") (1 g.) was added portionwise in 20 minutes at 25° to acetanilide (2·7 g.) in concentrated sulphuric acid (20 ml.). After a further 30 minutes at 25° the mixture was poured into ice and water (150 ml.). The precipitate was collected and (without preliminary drying) crystallised twice from alcohol, to yield the *nitramine* as needles (0·6 g.), m. p. 236° (Found: C, 60·3; H, 5·8; N, 15·5. $C_{18}H_{20}O_4N_4$ requires C, 60·6; H, 5·6; N, 15·7%).

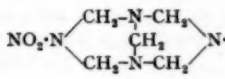
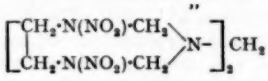
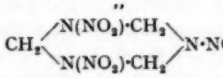
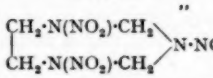
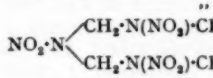
Di-p-*aminobenzylnitramine*.—Di-*p*-acetamidobenzylnitramine (0·5 g.) was heated under reflux for 1 hour with concentrated hydrochloric acid (5 ml.) and ethanol (5 ml.). The *dihydrochloride* of di-*p*-aminobenzylnitramine separated from the hot solution and recrystallised

from concentrated hydrochloric acid as platelets (0·35 g.), decomp. when heated (no m. p.) (Found: C, 48·7; H, 5·2; N, 16·6; Cl, 20·9. $C_{14}H_{18}O_2N_4Cl_2$ requires C, 48·7; H, 5·2; N, 16·3; Cl, 20·6%). The salt was dissolved in water, and basified with sodium hydroxide. The precipitated *di*-p-*aminobenzylnitramine* crystallised from alcohol in colourless plates, m. p. 157°, becoming brown on exposure to the air [Found: C, 61·5; H, 5·7; N, 20·2%; *M* (Rast), 283. $C_{14}H_{16}O_2N_4$ requires C, 61·8; H, 5·9; N, 20·5%; *M*, 272].

Di-p-*acetamidobenzylamine*.—Di-*p*-acetamidobenzylnitramine (0·5 g.) was heated for 2·5 hours under reflux with glacial acetic acid (5 ml.) and zinc dust (1 g.). After cooling, the excess of zinc was removed, and the filtrate diluted with water, basified with sodium hydroxide, washed with ether, and extracted with chloroform. Evaporation of the chloroform yielded a glassy solid (m. p. 50—60°) which could not be purified, but which was converted into the *hydrochloride* (needles which charred on being heated) by crystallisation from 2N-hydrochloric acid (Found: C, 59·1; H, 6·7; N, 11·4; Cl, 9·5. $C_{18}H_{22}O_2N_2Cl$ requires C, 62·1; H, 6·3; N, 12·1; Cl, 10·2%). The smallness of the yield made full purification impossible.

Di-p-*aminobenzylamine*.—Di-*p*-acetamidobenzylnitramine (0·5 g.) was heated under reflux for 2·5 hours with tin (1 g.) and concentrated hydrochloric (10 ml.). The solution was then cooled, basified with aqueous sodium hydroxide, and extracted with ether. Evaporation yielded a brown oil, which was converted into the trihydrochloride (Strakosch, *Ber.*, 1873, **6**, 1060) by dissolution in alcohol and addition of a small volume of concentrated hydrochloric acid (Found, after crystallisation from concentrated hydrochloric acid: C, 49·7; H, 6·0; N, 12·4; Cl, 31·7. Calc. for $C_{14}H_{20}N_2Cl_2$: C, 49·9; H, 5·9; N, 12·4; Cl, 31·7%). The base was regenerated from the purified salt and, crystallised from *cyclo*hexane, had m. p. 105° and was

TABLE 4. *Action of nitrated methylenediamines (aminomethylnitramines and polynitramines) on acetanilide in sulphuric acid of (a) 95·2% and (b) 99·7% w/w.*

Ref. no.	*N*-Nitro-compound	Yield (%) of $NO_2{\cdot}C_6H_4{\cdot}NHAc$	Other products isolated
25*a*	$NO_2{\cdot}NH{\cdot}CH_2{\cdot}NH{\cdot}NO_2$	nil	Compounds (I) (0·05 g.) and (II) (0·09 g.)
26*a*	$NO_2{\cdot}NAc{\cdot}CH_2{\cdot}NAc{\cdot}NO_2$	nil	Compounds (I) (0·1 g.) and (II) (0·05 g.)
27*a*	$\{O{<}[CH_2]_2{>}N{\cdot}CH_2{\cdot}N(NO_2){\cdot}CH_2{\cdot}\}_2$	nil	Ph·NHAc, and compound (I) (0·04 g.)
28*a*	 (" D.P.T.")	nil	Compound (II) (0·18 g.)
28*b*	"	13	—
29*a*	$AcO{\cdot}[CH_2{\cdot}N(NO_2)]_3{\cdot}CH_2{\cdot}OAc$ (" B.S.X.")	nil	Compound (II) (0·65 g.)
29*b*	"	nil	Compound (II) (0·2 g.)
30*a*		1	Ph·NHAc
30*b*	"	22	—
31*a*	 (" Cyclonite ")	30	—
31*b*	"	45	—
32*a*	 (" Homocyclonite ")	nil	Compounds (I) (0·05 g. and (II) (0·37 g.)
32*b*	"	14	—
33*a*	 (" H.M.X.")	1	Compound (II) (0·04 g.)
33*b*	"	18	Compound (II) (0·1 g.)

Note: The condensation products (I) and (II) were isolated (except in experiments 33*a*, 33*b*) by repeated fractional crystallisation of the initial ppt. from alcohol, in which (I) was the more soluble. In experiments 33*a* and *b* the initial ppt. was warmed with ethyl acetate: after cooling, compound (II) was collected and crystallised from alcohol. The ethyl acetate mother-liquor was evaporated, and *p*-nitroacetanilide isolated in the usual manner. The yields quoted in all cases are of the purified materials, m. p. 233° (I) and 236° (II).

identical in all respects with material synthesised from *p*-nitrobenzyl chloride by Strakosch's method (*loc. cit.*).

N-iso*Propylnitrourethane.*—*iso*Propylurethane (9 ml.) was added dropwise at −5° to nitric acid (15 ml.; 98%): the reaction readily became out of control if the temperature was allowed to rise. After the addition was complete the solution was poured at once into aqueous sodium carbonate (500 ml.) and extracted with ether. The extract yielded N-iso*propylnitrourethane* (10·5 g.; b. p. 84—85°/11 mm.) on drying and distillation (Found: C, 41·2; H, 7·1; N, 15·6%. $C_6H_{12}O_4N_2$ requires C, 40·9; H, 6·8; N, 15·9%). Curry and Mason (*J. Amer. Chem. Soc.*, 1951, **73**, 5045) have since reported b. p. 72°/7 mm.

Ethyl N-Carbethoxynitraminoacetate.—This compound was prepared by the method of Hantzsch and Metcalfe (*Ber.*, 1896, **29**, 1680), who did not attempt its purification. Extraction with ether, washing with aqueous sodium hydrogen carbonate, and distillation *in vacuo* yielded the pure *nitramide* as an oil, b. p. 148—149°/14 mm. (Found: C, 38·5; H, 5·8; N, 12·5. $C_7H_{12}O_6N_2$ requires C, 38·2; H, 5·5; N, 12·7%).

NN′-*Toluene*-p-*sulphonylethylenedinitramine.*—*NN′*-Toluene-*p*-sulphonylethylenediamine (Howard and Marckwald, *Ber.*, 1899, **32**, 2041) (6 g.) was added to nitric acid (26 ml.; 76%), and concentrated sulphuric acid (9 ml.) added dropwise at 0°. The mixture was poured into ice and water (250 ml.), and the resultant precipitate recrystallised from moist acetone, to yield NN′-*toluene*-p-*sulphonylethylenedinitramine* (4·5 g.) as needles, m. p. 176° (decomp.) (Found: C, 41·8; H, 4·0; N, 12·4; S, 13·9. $C_{16}H_{18}O_8N_4S_2$ requires C, 41·9; H, 3·9; N, 12·2; S, 14·0%).

2 : 7-*Dicyano*-2 : 7-*dimethyl*-3 : 6-*diazaoctane.*—Anhydrous ethylenediamine (3 ml.) was added dropwise in 20 minutes to acetone cyanohydrin (8·5 ml.), with cooling to keep the temperature below 60°. On cooling to 0° the liquid solidified. The solid was washed with ligroin (b. p. 40—60°), dissolved in *cyclo*hexane, freed from insoluble material by filtration, and allowed to crystallise by evaporation of the solvent. Recrystallisation from *cyclo*hexane yielded the dicyanodimethyldiazaoctane (6 g.; m. p. 56°). Jacobson (*J. Amer. Chem. Soc.*, 1945, **67**, 1996) gives m. p. 56°.

2 : 7-*Dicyano*-2 : 7-*dimethyl*-3 : 6-*dinitro*-3 : 6-*diazaoctane.*—2 : 7-Dicyano-2 : 7-dimethyl-3 : 6-diazaoctane (10 g.) was added with stirring to a mixture of acetic anhydride (48 ml.), acetyl chloride (1·5 ml.), and nitric acid (7·3 ml.; 100%) in 10 minutes at −50°. The dicyanodimethyldiazaoctane went into solution, and a fresh precipitate (probably a nitrate) soon separated. The reaction mixture was allowed to warm to 0° and, after 10 minutes at 0°, was set aside for 24 hours at 25° before being poured into ice and water (1400 ml.). The precipitate was collected, washed successively with water, alcohol, and ether, and crystallised from nitromethane (75 ml.), to yield the *dinitro*-compound as prismatic plates (6·8 g.), m. p. 212° (decomp.) (Found: C, 42·5; H, 5·8; N, 30·0. $C_{10}H_{16}O_4N_6$ requires C, 42·3; H, 5·6; N, 29·6%).

Other Compounds.—The remainder of the compounds used were furnished to us, or were prepared by known methods. Experiment numbers (from Tables 1, 2, or 3, and 4) and relevant references are: 3, McKay, *J. Amer. Chem. Soc.*, 1949, **71**, 1968; 5, Davis and Blanchard, *ibid.*, 1929, **51**, 1790; 6, Brian and Lamberton, *J.*, 1949, 1633; 7, Franchimont, *Rec. Trav. chim.*, 1894, **13**, 308; 10, Bachmann *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 3132; 11, Woodcock, *J.*, 1949, 1635; 12, Franchimont, *Rec. Trav. chim.*, 1902, **21**, 49; see Homeyer, *Chem. Abs.*, 1946, **40**, 4084, for initial amide; 13, as for 10; 14 and 15, Gillibrand and Lamberton, *J.*, 1949, 1883; 17, as for 10; 18, Wright *et al.*, *Canad. J. Res.*, 1948, **26**, *B*, 89; 19, Backer, *Rec. Trav. chim.*, 1912, **31**, 172; 20, 21, and 22, Wright *et al.*, *Canad. J. Res.*, 1948, **26**, *B*, 114; 25 and 26, as for 6; 27, as for 11; 28, Wright *et al.*, *Canad. J. Res.*, 1949, **27**, *B*, 218; 29, Bachman and Sheehan, *J. Amer. Chem. Soc.*, 1949, **71**, 1942; 30 and 32; Myers and Wright, *Canad. J. Res.*, 1949, **27**, *B*, 489.

We thank Dr. T. M. Walters for the provision of ethylenedinitramine and the compounds used in experiments nos. 2, 4, 31, and 33; and also for instructions regarding the preparation of the cyanomethylnitramine used in experiment 23.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, November 13th*, 1951; *revised, February 11th*, 1952.]

348. *Lanthanon Complexes with Ethylenediamine-NNN'N'-tetra-acetic Acid. Part III.**

By R. C. Vickery.

Stability constants have been derived for complexes of some lanthanons with ethylenediaminetetra-acetic acid. They increase from 15·3 for the lanthanum complex to 18·7 for the ytterbium complex, the constant of 18·0 for the yttrium complex being between those for dysprosium and erbium. Values for the free energies of formation of these complexes have been derived, and some conclusions drawn on the probable structure of the complexed molecules.

Stability constants for several bivalent-ion chelate systems have been given by various workers (*e.g.*, Schwarzenbach *et al.*, *Helv. Chim. Acta*, 1945, **28**, 828, *et seq.*; Maley and Mellor, *Aust. J. Sci. Res.*, 1949, **2**, 92, 579) but few determinations have been made of the constants of the various tervalent lanthanon chelate systems. A knowledge of these constants is of considerable value in separations of the lanthanons based on their ethylenediaminetetra-acetic acid ("enta") complexes, and it was for this reason that the determinations were made.

Adaptation of Bjerrum's theory of step equilibria ("Metal Ammine Formation in Aqueous Solutions," Copenhagen, 1941) to the derivation of stability constants of complex cations requires the solution of expressions for n (the average number of ligands, A, attached to the metal, M) and log 1/[A]. Maley and Mellor (*loc. cit.*) have generalised the form of derivation of these expressions from which are constructed the formation curves of the systems (the plot of n against log 1/[A]). From these curves the step-equilibria constants can be obtained and may be combined to yield the overall stability constant K.

The step equilibria normally involved in complex systems are

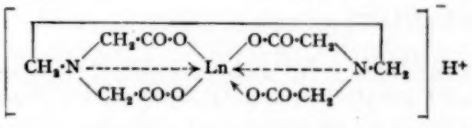
$$[MA]/[M][A] = k_1 \quad [MA_2]/[MA][A] = k_2$$
$$[MA_3]/[MA_2][A] = k_3, \text{ etc.} \qquad K = k_1k_2k_3 \ldots, \text{ etc.}$$

but Schwarzenbach has pointed out (*Nature*, 1951, **167**, 434) that bonds between a polydentate ligand and a metal are formed simultaneously and that only complexes involving more than one ligand mole per metal ion are formed stepwise. In the lanthanon–"enta" systems therefore the reaction is $Ln^{3+} + H_4A \longrightarrow LnHA + 3H^+$ giving $K = [LnHA]/[Ln^{3+}][HA^{3-}]$.

"Enta" (I) forms complexes with the lanthanons as in (II). Zwitterion characteristics

(I) $[\cdot CH_2\cdot N(CH_2\cdot CO_2H)_2]_2$ (III) $[\cdot CH_2\cdot \overset{+}{N}H(CH_2\cdot CO\cdot \bar{O})]_2$

(II)



have been attributed to "enta," for Long, Jones, and Burke (Brookhaven Chemical Conf., No. 2, 1948, 106) and Schwarzenbach (*loc. cit.*) have represented it as (III), but the zwitterion would not be expected to promote complex formation because of the positive charge on the nitrogen atom. An equilibrium would exist between the zwitterion and "enta" and the effect of zwitterion formation would be to reduce the rate of complex formation. However, since "enta" may be titrated as a tetrabasic acid, Schwarzenbach claims that the zwitterion effect may be disregarded in calculations of stability constants. The pK_a values for "enta" (Schwarzenbach, *loc. cit.*) would appear to confirm this, *viz.*, pK_1, 1·996; pK_2, 2·672; pK_3, 6·161; pK_4, 10·262. Joy, however (private communication), considers that this zwitterion effect cannot be so disregarded, for it

* Part II, *J.*, 1952 421.

becomes of increasing importance with increase in pH of the system above *ca.* 6·0. Since it is now found that in dilute solutions some 90% of the lanthanon–" enta " chelation occurs below pH 6·0, for the purpose of this work we may disregard the zwitterion characteristics of " enta " and be concerned only with the relationships between (I) and (II).

Conventions and Derivations (all concentrations in moles/litre).

T_{Ln} = Concentration of total lanthanons in system.

T_A = Concentration of total " enta " in all forms in system.

T_H = Concentration of total ionised and potentially ionisable hydrogen in system.

n_A = (Total potentially ionisable hydrogen bound to " enta ")/(Total " enta " unattached to lanthanons).

α = (" Enta " unattached to lanthanons or hydrogen)/(Total " enta " unattached to lanthanons).

n = (" Enta " attached to lanthanons)/T_{Ln}.

E = Initial concentration of strong acid (normality).

Q = Added strong alkali.

The four dissociation constants of " enta," K_1, K_2, K_3, K_4, follow from Schwarzenbach's pK values (above), and, on introduction of the various species concerned, we have :

$$T_{Ln} = [Ln^{3+}] + [LnHA]$$

$$T_A = [A^{4-}] + [HA^{3-}] + [H_2A^{2-}] + [H_3A^-] + [H_4A] + nT_{Ln}$$

$$T_H = [H^+] + [HA^{3-}] + 2[H_2A^{-2}] + 3[H_3A^-] + 4[H_4A] + nT_{Ln}$$

$$n_A = \frac{[HA^{3-}] + 2[H_2A^{2-}] + 3[H_3A^-] + 4[H_4A]}{[A^{4-}] + [HA^{3-}] + [H_2A^{2-}] + [H_3A^-] + [H_4A]}$$

$$\alpha = [A^{4-}]/([A^{4-}] + [HA^{3-}] + [H_2A^{2-}] + [H_3A^-] + [H_4A])$$

$$n = T_A - ([A^{4-}] + [HA^{3-}] + [H_2A^{2-}] + [H_3A^-] + [H_4A])/T_{Ln}$$

$$T_A = (T_H - [H^+] - nT_{Ln})/n_A + nT_{Ln}$$

Since " enta " has four dissociable hydrogens, we have $T_H = (E - Q) + K_w/[H^+] + 4T_A$ and substitution of dissociation constants for " enta " in n_A gives

$$n_A = \frac{[A^{4-}][H^+]/K_4 + 2[HA^{3-}][H^+]/K_3 + 3[H_2A^{2-}][H^+]/K_2 + 4[H_3A^-][H^+]/K_1}{K_4[HA^{3-}]/[H^+] + [A^{4-}][H^+]/K_4 + [HA^{3-}][H^+]/K_3 + [H_2A^{2-}][H^+]/K_2 + [H_3AH^+]/K_1^-][}$$

Dividing through by $[HA^{3-}]$, we have

$$n_A = \frac{1 + 2[H^+]/K_3 + 3[H^+]^2/K_2K_3 + 4[H^+]^3/K_1K_2K_3}{1 + K_4/[H^+] + [H^+]/K_3 + [H^+]^2/K_2K_3 + [H^+]^3/K_1K_2K_3}$$

Similarly

$$\alpha = \frac{K_4/[H^+]}{1 + K_4/[H^+] + [H^+]/K_3 + [H^+]^2/K_2K_3 + [H^+]^3/K_1K_2K_3}$$

$$n = \frac{T_A - \left(\frac{(E - Q) + K_w/[H^+] + 4T_A - [H^+] - nT_{Ln}}{n_A}\right)}{T_{Ln}}$$

$$= \frac{T_A\left(1 - \frac{4}{n_A}\right) - \frac{(E - Q) + K_w/[H^+] - [H^+] - nT_{Ln}}{n_A}}{T_{Ln}}$$

$$[A] = \alpha(T_H - [H^+])/n_A - nT_{Ln} = \alpha\{(E - Q) + K_w/[H^+] + 4T_A - [H^+] - nT_{Ln}\}/n_A$$

Values thus obtained for n and log $1/[A]$ are plotted against each other to give the formation curve, and $K = [LnHA]/[Ln^{3+}][HA^{3+}]$ is extracted, as the value when $n = 0{\cdot}5$, *i.e.*, when there are equal amounts of $LnHA_{x-1}$ and $LnHA_x$ present (Bjerrum, *loc. cit.*).

Fig. 1 shows the pH curves for titration of lanthanon–" enta " systems with standard alkali, and Fig. 2 the formation curves obtained from data yielded by the titrations. The table records the K values extracted from the formation curves at $n = 0{\cdot}5$. Titration and formation curves and K values are also included for the yttrium–" enta " system. The gadolinium–" enta " system gave a titration curve identical with that of the samarium–" enta " system and is not therefore shown, nor is its formation curve plotted. Within experimental error, the constant K for gadolinium is considered to be identical with that for samarium.

The increase in K values for the lanthanon–" enta " systems parallels the increase in atomic number through the lanthanon series, with yttrium coming between dysprosium

FIG. 1. *Titration curves for lanthanon–enta systems.*

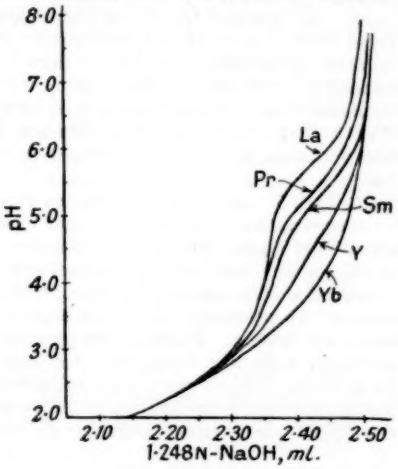
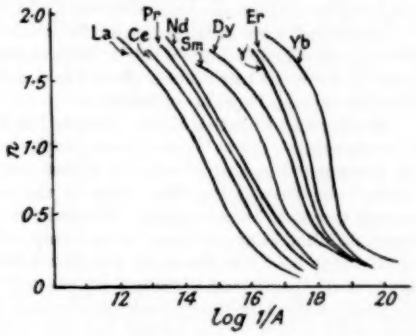


FIG. 2. *Formation curves for lanthanon–enta systems.*



and erbium at about the position of holmium. The value for lanthanum is in good agreement with Schwarzenbach's value (*Helv. Chim. Acta*, 1951, **34**, 1503) of $15{\cdot}4 \pm 0{\cdot}05$, and the situation of yttrium between dysprosium and erbium is in keeping with the sequence obtained during separation of the lanthanons by decomposition of their " enta " complexes (Marsh, *J.*, 1950, 1819).

Since the ligand–metal reaction is in this instance one-step and the ligand sexadentate, the " characteristic co-ordination number " Z (Bjerrum) is 6. We may therefore expect the complex to have an octahedral configuration with the ligand bound exclusively in the form of five-membered chelate rings (Bjerrum, *Chem. Reviews*, 1950, **46**, 381).

Employing Bjerrum's quantity (*loc. cit.*) $(N/Z)\log K + \log 55$, we may easily derive the free energies of complex formation of the lanthanon–" enta " chelates. These are given also in the table. The only data available for comparison are those given by Bjerrum for

Overall stability constants and free energies of formation of lanthanon–enta complexes.

Lanthanon	log K	(N/Z) log K + log 55	Lanthanon	log K	(N/Z) log K + log 55	Lanthanon	log K	(N/Z) log K + log 55
La	15·30	4·29	Sm	17·2	4·61	Er	18·15	4·77
Ce	16·05	4·41	Gd			Yb	18·70	4·85
Pr	16·55	4·50	Dy	17·75	4·70	Y	18·0	4·74
Nd	16·75	4·53						

La–OH and La–SO_4 systems which are ~5 and 3·7, respectively. The values given represent only measures of the change in free energy on complex formation and must be multiplied

by 1·362 to give the results in kcals. at 25°. Values of K or of free-energy change for lanthanon complexes with ethylenediamine, ammonia, or acetates are not known, and it is not therefore possible to derive information concerning the increase of stability arising from chelation in the lanthanon–" enta " system as compared with other lanthanon systems.

Plumb, Martell, and Bersworth (*J. Phys. Coll. Chem.*, 1950, **54**, 1208), employing spectrophotometry, derived values for the relative strengths of " enta " complex formation with metal ions. The values they obtained were, however, somewhat empirical and took Cu = 100 as the standard : this gave a value of 300 for Cr and 39 for Ni at pH 4·00. Such values are much distorted in comparison with those obtained titrimetrically, but the data given by these workers do show clearly the effect of pH on the location of a metal ion in the stability series, thus affording confirmation of the zwitterion effect noted above.

Experimental

The lanthanons employed were of the purities indicated in Part II of this series (*loc. cit.*) and the " enta " employed was the analytical " Sequestrene " AA grade of the Alrose Chemical Co., Providence, U.S.A. This " enta " was further purified before use by two crystallisations from water and a final precipitation from ammoniacal solution by acidification. The " enta " was prepared as M/1000-aqueous solution and the lanthanons as M/100-nitrate solutions.

Titrations were carried out at 20° with 1·248N-sodium hydroxide (carbonate free) against 100 ml. of solution $0·98 \times 10^{-3}$M with regard to " enta," $0·2 \times 10^{-5}$M to lanthanon ion, and $2·563 \times 10^{-3}$N to nitric acid, the ionic concentrations of the system being maintained at 0·1M by addition of potassium chloride.

Moeller and Brantley (Univ. Illinois N6OR-71 Chem. Task 7, Sept. 1949), in titration studies of neodymium–" enta " complexes, employed higher concentration of neodymium than used in the present work, and what were considered correspondingly higher effective concentrations of " enta " by suspending the latter in the neodymium solution and stirring mechanically for several minutes before taking pH readings. This method is insufficiently accurate, however, when stability constants are to be computed, because of the possibility of non-attainment of equilibrium between the solid and the liquid phase of the system. Further, the presence in solution of insufficient " enta " to convert the lanthanon fully into complex could lead to titration of the lanthanon itself (as distinct from the complex) thereby precipitating lanthanon hydroxide, which would extend the time required for attainment of equilibrium in the system. In this work it was considered preferable to employ fully solvated " enta " even though higher dilutions of lanthanon ions had to be employed.

pH measurements obtained on a Cambridge pH meter were taken as measurements of hydrogen-ion concentrations in the system, no account being taken of activity coefficients. A simple calculation showed that this did not lead to an appreciable variation in the formation curve functions.

The author thanks Mr. A. S. Joy and Mr. F. R. Hartley for assistance in deriving the stability constants reported in this work, which was started in England and completed as part of the research programme of this Division of C.S.I.R.O.

Division of Industrial Chemistry,
Commonwealth Scientific & Industrial Research Organization,
Box 4331, G.P.O., Melbourne. [*Received, September 18th*, 1951.]

349. *Acenaphthyleno-compounds. Part II.**

By J. B. Duthie and S. G. P. Plant.

The ease with which acenaphthenone undergoes self-condensation to 8-acenaphthylideneacenaphthen-7-one has prevented its use in some well-known reactions of the $-CH_2 \cdot CO-$ group. Nevertheless, ethyl 8-ketoacenaphthene-7-glyoxylate has been prepared and used for the synthesis of derivatives of acenaphthyleno(7′ : 8′-4 : 5)pyrazole. Acenaphthyleno-compounds in general have been found not readily to undergo polymerisation at 300°, but methyl acenaphthyleno(7′ : 8′-2 : 3)indole-1-carboxylate gave 1-methylacenaphthyleno(7′ : 8′-2 : 3)indole and carbon dioxide.

The results described in a previous communication * indicate that interest attaches to compounds which contain the acenaphthylene system fused to other cyclic structures. Acenaphthenone (I; R = H) appears to be a convenient starting point for the preparation of some of these substances, and Sircar and Gopalan (*J. Indian Chem. Soc.*, 1932, **9**, 297) have obtained acenaphthyleno(7′ : 8′-2 : 3)quinoline (II) from it by condensation with *o*-aminobenzaldehyde (see also Buu-Hoï and Cagniant, *Compt. rend.*, 1943, **216**, 447). Attempts have now been made to prepare the quinolone (III) by heating the ketone (I; R = H) with anthranilic acid, an application of Niementowski's reaction (*Ber.*, 1894, **27**, 1394; see also Tiedtke, *Ber.*, 1909, **42**, 621), but the ketone was readily converted under these conditions into 8-acenaphthylideneacenaphthen-7-one (IV) by a self-

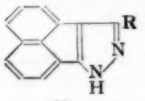
(I) (II) (III) (IV)

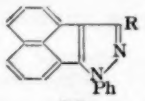
condensation process. This is reminiscent of observations by Blount and Plant (*J.*, 1937, 376) who found that *cyclo*pentanone was converted first into *cyclo*pentylidene*cyclo*pentanone in a similar experiment. An alternative route to (III) would be from aniline and ethyl 8-ketoacenaphthene-7-carboxylate (I; R = CO_2Et), but efforts to obtain the latter have been unsuccessful. Ethyl 8-ketoacenaphthene-7-glyoxylate (I; R = $CO \cdot CO_2Et$) has been prepared from (I; R = H) and ethyl oxalate in ethanolic sodium ethoxide, but it did not give (I; R = CO_2Et) on pyrolysis under a variety of conditions. Only 8-acenaphthylideneacenaphthen-7-one was obtained in attempts to condense acenaphthenone with ethyl carbonate in the presence of sodium ethoxide, and similar results attended efforts to prepare (I; R = CHO) with ethyl formate under analogous conditions.

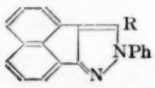
The ester (I; R = $CO \cdot CO_2Et$) might form the starting point for the preparation of various heterocyclic substances, and ethyl acenaphthyleno(7′ : 8′-4 : 5)pyrazole-3-carboxylate (V; R = CO_2Et), obtained from it by the action of hydrazine, has been converted through the acid (V; R = CO_2H) into acenaphthyleno(7′ : 8′-4 : 5)pyrazole (V; R = H). A similar reaction with phenylhydrazine has given an analogous product for which two structures (VI and VII; R = CO_2Et) are possible (the corresponding forms of the product from hydrazine would be readily interconvertible as tautomerides). The same structural problem arose with the substance obtained by Beyer and Claisen (*Ber.*, 1887, **20**, 2178) from phenylhydrazine and ethyl benzoylpyruvate, $Ph \cdot CO \cdot CH_2 \cdot CO \cdot CO_2Et$, but this was shown to be ethyl 1 : 5-diphenylpyrazole-3-carboxylate by the fact that it was also prepared by the action of benzenediazonium chloride on ethyl α-phenacylacetoacetate, $CH_3 \cdot CO \cdot CH(CH_2 \cdot CO \cdot Ph) \cdot CO_2Et$ (Bischler, *Ber.*, 1892, **25**, 3143), and by analogy the above product is regarded as (VI; R = CO_2Et). An attempt to establish this structure in a way analogous to that of Bischler has failed, since it has been found by Mr. M. F. A. Jones in this laboratory that the action of 8-bromoacenaphthen-7-one

* The paper by Bannister and Plant, *J.*, 1948, 1247, is considered as Part I.

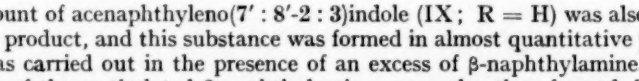
(I; R = Br) on the sodium derivative of ethyl acetoacetate under some conditions leads to the formation of the compound (VIII).


(V)

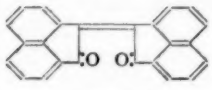

(VI)

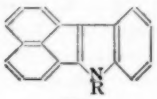

(VII)

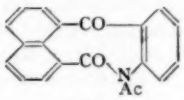
Pyrolysis of the acid (VI; R = CO_2H) gave results which appeared to be fortuitous. The product was difficult to purify, but in some experiments a red compound, $C_{19}H_{12}N_2$, presumably (VI; R = H) although it was different in appearance from (V; R = H), was obtained. On one occasion a compound, m. p. 316° (decomp.), which appeared to have the composition $C_{39}H_{24}O_2N_4$, formed from equimolecular amounts of (VI; R = H) and (VI; R = CO_2H), was isolated. Acenaphthylene is rapidly polymerised by heat (Dziewoński and Leyko, *Ber.*, 1914, **47**, 1679), and it seemed possible that polymerisation might be effected in this series. A number of acenaphthyleno-compounds were accordingly heated at temperatures of about 300° for approximately 10 minutes. The substances (V; R = CO_2Et), (V; R = H), (VI; R = CO_2Et), (IX; R = H), (IX; R = Me), and (IX; R = Ac) were essentially unchanged in this way. Methyl acenaphthyleno(7′ : 8′-2 : 3) indole-1-carboxylate (IX; R = CO_2Me) also gave no polymer, but it decomposed to give carbon dioxide and a substantial quantity of 1-methylacenaphthyleno(7′ : 8′-2 : 3)-indole (IX; R = Me). This reaction may be represented by the scheme:



A small amount of acenaphthyleno(7′ : 8′-2 : 3)indole (IX; R = H) was also isolated from the reaction product, and this substance was formed in almost quantitative yield when the pyrolysis was carried out in the presence of an excess of β-naphthylamine. Presumably one or more of the methylated 2-naphthylamines were also then formed, but they could not be purified or identified. It is of interest in this connexion that Nölting (*Ber.*, 1888, **21**, 3154) obtained aniline, methylaniline, and dimethylaniline from the product of heating methyl phenylcarbamate, Ph·NH·CO_2Me, with lime at 260°.


(VIII)


(IX)


(X)

Koelsch (*J. Amer. Chem. Soc.*, 1944, **66**, 1983) found that 1-acetyl-6-bromo-2 : 3-diphenylindole could be oxidised by chromic acid in acetic acid solution to *N*-acetyl-2-benzoyl-5-bromobenzanilide, and the process has been extended by other workers to several indole derivatives. It has now been found that the same reaction can be applied to 1-acetylacenaphthyleno(7′ : 8′-2 : 3)indole (IX; R = Ac) with the formation of *o*-(8-carboxy-1-naphthoyl)acetanilide lactam (X).

Experimental

Action of Anthranilic Acid on Acenaphthenone.—After a mixture of anthranilic acid (2 g.) and acenaphthenone (2 g.) had been heated at 100° for 2 hours, the product was cooled, pulverised, and digested with ethanol (100 c.c.). When the residue (1·5 g.) was crystallised from acetone, yellow needles (1·1 g.; nitrogen free; m. p. 247°) were isolated, and these were further purified by adsorption from benzene on alumina. The 8-acenaphthylideneacenaphthen-7-one obtained (1 g.) then crystallised from chloroform in yellow needles, m. p. 262° (Found: C, 90·5; H, 4·5. Calc. for $C_{24}H_{14}O$: C, 90·6; H, 4·4%) (Graebe and Jequier, *Annalen*, 1896, **290**, 202, give m. p. 262°).

Ethyl 8-Ketoacenaphthene-7-glyoxylate.—A suspension of acenaphthenone (16·8 g.) in ethyl oxalate (150 c.c.) was added during 10 minutes with mechanical stirring to a solution of sodium

(2·5 g.) in dry ethanol (35 c.c.) kept below 10°. Stirring was continued for 2 hours at 0—5°, and an orange solid separated. While the mixture was still cold, concentrated sulphuric acid (3 c.c.)–ice (25 g.) was carefully added, and the whole poured into water (500 c.c.). When the solid was crystallised from ethanol, *ethyl 8-ketoacenaphthene-7-glyoxylate* (23 g.) was obtained in yellow plates, m. p. 104° (Found: C, 71·8; H, 4·4. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). It was readily dissolved by dilute aqueous sodium hydroxide, and its solution in ethanol gave an intense blue colour with ferric chloride.

Acenaphthyleno(7′ : 8′-4 : 5)*pyrazole*.—A solution of ethyl 8-ketoacenaphthene-7-glyoxylate (5·36 g.) and hydrazine hydrate (1·12 g. of 90%) in glacial acetic acid (40 c.c.) was boiled under reflux for 15 minutes in darkness, and, when cold, stirred into ice-water (1 l.). After 6 hours, the yellow solid was collected and crystallised from ethanol, from which *ethyl acenaphthyleno*(7′ : 8′-4 : 5)*pyrazole-3-carboxylate* separated in yellow needles (5·1 g.), m. p. 163° (Found: C, 72·4; H, 4·6. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·5%). Further purification by adsorption from benzene on alumina did not change the colour or the m. p. When the reaction was carried out in daylight, the crude product was red and difficult to purify.

A solution of the ester (9 g.) in ethanol (400 c.c.) was boiled under reflux while concentrated aqueous sodium hydroxide was added dropwise until a test portion of the mixture no longer gave a turbidity with water. After a further ½ hour, most of the ethanol was distilled off, and the cold residue acidified with hydrochloric acid. The precipitate which slowly separated was dissolved in hot ethanol (125 c.c.), and the addition of water (12 c.c.) then caused the separation of *acenaphthyleno*(7′ : 8′-4 : 5)*pyrazole-3-carboxylic acid* in colourless plates (8 g.), m. p. 289° (decomp.) (Found: C, 70·8; H, 3·5. $C_{14}H_8O_2N_2$ requires C, 71·2; H, 3·4%). After the acid (1 g.) had been heated at 310° for 5 minutes, the product was cooled, pulverised, and extracted with ethanol (150 c.c.) in a Soxhlet apparatus. The extract was boiled with charcoal, filtered, and concentrated, and, on cooling, *acenaphthyleno*(7′ : 8′-4 : 5)*pyrazole*, colourless needles (0·5 g.; from ethanol), m. p. 239°, slowly separated (Found: C, 81·2; H, 4·3%; *M* (Rast), 210. $C_{13}H_8N_2$ requires C, 81·3; H, 4·2%; *M*, 192).

When this product (0·5 g.) was heated under reflux with acetic anhydride (10 c.c.) for ½ hour and the solution poured into water, *1-acetylacenaphthyleno*(7′ : 8′-4 : 5)*pyrazole*, pale straw-coloured plates (0·45 g.; from ethanol), m. p. 170—171°, was precipitated (Found: C, 76·8; H, 4·3. $C_{15}H_{10}ON_2$ requires C, 76·9; H, 4·3%). Its solutions in benzene and ethanol were colourless.

1-Phenylacenaphthyleno(7′ : 8′-4 : 5)*pyrazole-3-carboxylic Acid*.—A mixture of purified phenylhydrazine (2·16 g.), ethyl 8-ketoacenaphthene-7-glyoxylate (5·36 g.), and glacial acetic acid (30 c.c.) was refluxed for 2½ hours in darkness, cooled, and poured into ice-water (500 c.c.); the precipitated *ethyl 1-phenylacenaphthyleno*(7′ : 8′-4 : 5)*pyrazole-3-carboxylate* crystallised from ethanol in yellow plates (4·8 g.), m. p. 161° (Found: C, 77·6; H, 4·8%; *M* (Rast), 308. $C_{22}H_{16}O_2N_2$ requires C, 77·6; H, 4·7%; *M*, 340). When this substance was saponified by the method described above for the related ester, the sodium salt gradually separated from the ethanol solution. Acidification of its solution in water precipitated *1-phenylacenaphthyleno*(7′ : 8′-4 : 5)-*pyrazole-3-carboxylic acid*, colourless needles (yield, 85%; from aqueous ethanol), m. p. 262° (decomp.) (Found: C, 76·7; H, 3·9. $C_{20}H_{12}O_2N_2$ requires C, 76·9; H, 3·8%).

When the acid (1 g.) was heated at 265° until effervescence ceased (about ½ minute), the nature of the product varied in different experiments. On four occasions nothing pure was isolated, and twice *1-phenylacenaphthyleno*(7′ : 8′-4 : 5)*pyrazole*, a microcrystalline scarlet solid (yield, 0·5 g. and 0·1 g. respectively; from glacial acetic acid), m. p. 197°, was obtained (Found: C, 84·8; H, 4·3; N, 10·6. $C_{19}H_{12}N_2$ requires C, 85·1; H, 4·5; N, 10·4%). On one occasion a *substance*, $C_{39}H_{24}O_2N_4$, golden-brown needles (0·5 g.; from glacial acetic acid), m. p. 316° (decomp.), was isolated (Found: C, 80·6, 80·6; H, 4·2, 4·3. $C_{39}H_{24}O_2N_4$ requires C, 80·7; H, 4·1%). These last two substances were not sufficiently soluble in camphor for molecular-weight determinations.

Pyrolysis of Methyl Acenaphthyleno(7′ : 8′-2 : 3)*indole-1-carboxylate*.—(*a*) When this urethane (1 g.; Bannister and Plant, *loc. cit.*) was heated at 300° for 10 minutes, carbon dioxide, identified with lime water, was evolved. The residue was refluxed with benzene (25 c.c.), and the hot solution filtered from insoluble material (0·1 g.), cooled, and diluted with more benzene (75 c.c.). The solute was adsorbed on alumina and separated into three fractions: (i) 1-methylacenaphthyleno(7′ : 8′-2 : 3)indole, scarlet plates (0·2 g.), m. p. 204° (Found: C, 88·7; H, 5·2; N, 6·0%; *M* (Rast), 277. Calc. for $C_{19}H_{13}N$: C, 89·4; H, 5·1; N, 5·5%; *M*, 255), identified by mixed m. p.; (ii) unchanged methyl acenaphthyleno(7′ : 8′-2 : 3)indole-1-carboxylate (0·5 g.), m. p. 154°; and (iii) acenaphthyleno(7′ : 8′-2 : 3)indole (0·05 g.), brown plates, m. p. 234°, identified

by mixed m. p. The same three substances were isolated in a number of similar experiments in varying yields which appeared to be unconnected with the time of pyrolysis (5—25 minutes).

(*b*) A mixture of the urethane (0·5 g.) and β-naphthylamine (2·5 g.) was heated under reflux at 300° for 10 minutes, cooled, and repeatedly ground with dilute hydrochloric acid until nothing more was extracted. When the residue was crystallised from ethanol, acenaphthyleno(7′ : 8′-2 : 3)indole was obtained in orange plates (0·4 g.), m. p. 234°, identified by mixed m. p.

Oxidation of 1-*Acetylacenaphthyleno*(7′ : 8′-2 : 3)*indole.*—A solution of the acetyl compound (5 g.) in boiling glacial acetic acid (250 c.c.) was rapidly cooled, with stirring, and treated with chromic anhydride (2·4 g.) in water (15 c.c.). The whole was shaken at 15—20° for 18 hours and then at 70° for 10 minutes, filtered from unchanged acetyl compound (1 g.), and gradually treated with water (3 l.), with stirring. After the orange-coloured precipitate (3 g.) had been recrystallised from methanol (twice) and then benzene, o-(8-*carboxy*-1-*naphthoyl*)*acetanilide lactam* was obtained in colourless prisms (0·6 g.), m. p. 184° (Found: C, 76·5; H, 4·1. $C_{20}H_{13}O_3N$ requires C, 76·2; H, 4·1%).

Dyson Perrins Laboratory, Oxford University. [*Received, January 11th,* 1952.]

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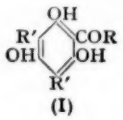
350. *The Chemistry of Hop Constituents. Part II.* Oxidation Products of Lupulone.*

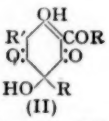
By G. A. Howard and J. R. A. Pollock.

A new oxidative degradation of lupulone is described, and structures are suggested for the new degradation products.

Lupulone, one of the bitter resins of the hop, was shown by Wöllmer (*Ber.*, 1916, **49**, 750; 1925, **58**, 672) to undergo hydrogenolysis, yielding 2-methylbutane and a compound believed to be represented by (I), which was then oxidised to "tetrahydrohumulone" (II). Alkaline hydrolysis of (II) gave 4-methylpentanoic acid† and dihydrohumulinic acid (III); the structure of (III) was considered incontrovertible. This degradation, considered with the lack of optical activity of lupulone, its empirical formula ($C_{26}H_{38}O_4$), and the similarity between "tetrahydrohumulone" and humulone, led Wöllmer (*loc. cit.*) to propose structure (IV) for lupulone. This structure has recently received further support by a synthesis of lupulone by trialkylation of 2 : 4 : 6-trihydroxy*iso*valerophenone with 1-bromo-3-methylbut-2-ene (Riedl, *Brauwissenschaft*, 1951, 133); although this greatly limits the possibilities it is not entirely unambiguous, as *O*-alkylation might well occur under the conditions used.



(I)



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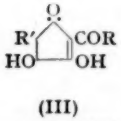

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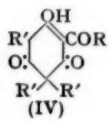


(IV)

R = CH_2·$CHMe_2$; R′ = CH_2·CH:CMe_2.

The present paper presents a new degradation of lupulone involving changes which do not involve the elimination of 2-methylbutane such as occurs during hydrogenolysis. Walker (*J. Inst. Brewing*, 1924, **30**, 712) has reported the stability of lupulone to aqueous alkali. It has now been shown that hydrogen peroxide in alkaline medium induces a rapid degradation in the cold, to a carboxylic acid, lupuloxinic acid, $C_{22}H_{32}O_5$, and *iso*-butyric acid. Lupuloxinic acid behaves as a strong dibasic acid (pK_1, 3·9; pK_2, 9·7) which causes effervescence in aqueous sodium hydrogen carbonate. It contains two active hydrogen atoms, shows an absorption maximum at 252 mμ (ε = 10,000 in ethanol), and gives no colour with ferric chloride solution. Lupuloxinic acid reduces one equivalent of periodate very rapidly and is unsaturated (tetranitromethane). By analogy with lupulone, it was thought that lupuloxinic acid might undergo loss of a C_5 fragment on hydrogenation;

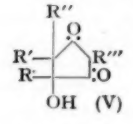
* Part I, *J.*, 1950, 1873.

† Geneva nomenclature (CO_2H = 1).

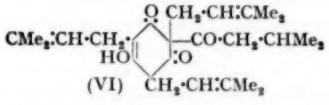
this was not the case, however, hexahydrolupuloxinic acid, $C_{22}H_{38}O_5$, being the main product of hydrogenation over palladium chloride. Together with hexahydrolupuloxinic acid, an enolic fraction was present, from which a crystalline substance, hexahydrolupulenol, $C_{21}H_{38}O_3$, was isolated. The latter was obtained as the main product when Adams's catalyst in dioxan–acetic acid was used. Hexahydrolupulenol contains two active hydrogen atoms and behaves as a weak monobasic acid. It gives a purple colour with ferric chloride solution, shows characteristic ultra-violet absorption at 250 (maximum) and 256 mμ (inflexion; $\varepsilon = 14{,}000$ and 12,000 respectively in ethanol), and rapidly reduces one equivalent of periodate. It forms a phenylurethane, which is, however, obtained only in poor yield. These properties indicate clearly that the relation of hexahydrolupulenol to hexahydrolupuloxinic acid is that of a β-diketone to the corresponding ββ′-diketocarboxylic acid. That lupuloxinic acid indeed possesses the latter structure is apparent from its very smooth decarboxylation in toluene, to yield lupulenol, $C_{21}H_{32}O_3$, the properties of which are very similar to those of its hexahydro-derivative. Thus lupulenol contains two active hydrogen atoms, behaves as a monobasic acid of pK 6·4, and gives a purple colour with ferric chloride solution. It possesses an absorption maximum at 253 mμ ($\varepsilon = 12{,}340$) and rapidly reduces one equivalent of periodate. Lupulenol is unsaturated (tetranitromethane), and on catalytic hydrogenation over Adams's catalyst absorbs the equivalent of six atoms of hydrogen, affording hexahydrolupulenol in excellent yield.

Periodate oxidation of lupulenol gives a resinous enolic acid which, on hydrolysis with sodium hydroxide, yields, as the major product, a compound, $C_{18}H_{30}O$. Although, by reason of its method of preparation and its lack of active hydrogen, this compound must necessarily be a ketone, it fails to react with 2 : 4-dinitrophenylhydrazine. It is unsaturated, and on hydrogenation yields its hexahydro-derivative, $C_{18}H_{36}O$, as an oil which also fails to form ketonic derivatives. Vigorous oxidation of this hexahydro-derivative gave 4-methylpentanoic acid, thus establishing the presence of the 4-methylpentanoyl or 5-methylhexanoyl group.

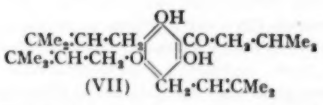
Since lupulenol and its hexahydro-derivative each contain three oxygen atoms, two of which are accommodated in a β-diketone system, and since each compound contains two active hydrogen atoms and reduces one equivalent of periodate, an α-ketol grouping must be present. Further, as both acids are stable to Fehling's solution, a tertiary hydroxyl group is indicated and, moreover, the ketol must be part of a ring system, otherwise its periodate oxidation would give rise to a simple ketone as a primary product. These facts are completely accommodated only by (V); alternative expressions are excluded as they would lead, on oxidation and hydrolysis, to stable diketones. The ketone, $C_{18}H_{30}O$, obtained from lupulenol must therefore be represented by R·CO·CHR′R″ where the most probable formulation for R is $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2$ and for R′ and R″ is $CMe_2{:}CH{\cdot}CH_2$. Lupulenol and its hexahydro-derivative thus become respectively (V; R = $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2$; R′ = R″ = $CMe_2{:}CH{\cdot}CH_2$; R‴ = H) and (V; R = $CHMe_2{\cdot}[CH_2]_3$; R′ = R″ = $CHMe_2{\cdot}[CH_2]_2$; R‴ = H). These formulations are compatible



(V)



(VI)



(VII)

with the formation of a monophenylurethane by hexahydrolupulenol. The similarity of the ultra-violet absorption spectra of lupulenol and hexahydrolupulenol shows that the double bonds of the former which are susceptible to hydrogenation are not conjugated; incidentally, the close similarity between the absorption of these compounds and that of 4-hydroxy-2-methyl*cyclo*pentane-1 : 3-dione (max., 249 mμ; $\varepsilon = 16{,}000$; Bastron, Davis, and Butz, *J. Org. Chem.*, 1943, **8**, 515), 2-methyl*cyclo*pentane-1 : 3-dione (max., 250 mμ; $\varepsilon = 18{,}000$; *idem, ibid.*), and 2-ethyl-4-*n*-propyl*cyclo*pentane-1 : 3-dione (max., 252 mμ; $\varepsilon = 14{,}450$; Blout, Eager, and Silverman, *J. Amer. Chem. Soc.*, 1946, **68**, 568) strongly supports the structures postulated. It follows from the foregoing that lupuloxinic acid must have the structure (V; R = $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2$; R′ = R″ =

CMe_2:$CH{\cdot}CH_2$; R''' = CO_2H), and that therefore for lupulenol R''' in formula (V) must be H.

Only the structures (V) now postulated for lupulenol and lupuloxinic acid satisfactorily explain all the properties of the compounds. It must be admitted, none the less, that a clear understanding of the mechanism whereby lupulone becomes transformed into lupuloxinic acid is not yet possible. The recent synthesis by Riedl (*loc. cit.*) was accepted by him as confirming the structure (IV) postulated by Wöllmer (*loc. cit.*). It should be pointed out, however, that the synthesis could equally well lead to (VI) or (VII), of which the latter seems the more acceptable, since it alone accommodates the hydrogenolysis of lupulone as a rational property of its structure.

Experimental

Lupulone and Humulone.—(a) *From hops.* The method of Lewis *et al.* (*J. Clin. Invest.*, 1949, **28**, 916) was adapted for the extraction of lupulone from hops. Ground, commercially dried cones of Bullion hops (4·91 kg.) were packed in columns (5 in. diameter × 9 in. high) and extracted by percolation with light petroleum (b. p. 40—80°; 10 l.). The percolates were dried ($CaCl_2$) and evaporated under nitrogen *in vacuo* at 40°, to leave a syrup (870 g.) from which lupulone crystallized on cooling to 0°. Recrystallization from light petroleum gave lupulone (75 g., 1·5% based on hops), m. p. 92—94° (Found : C, 75·0, 75·4, 75·6; H, 9·1, 9·4, 9·2; active H, 0·49%; I.V., 126·7; equiv. by titration, 404, 411. Calc. for $C_{26}H_{38}O_4$: C, 75·3; H, 9·2; 2 active H, 0·48%; I.V. for 2 double bonds, 123·7; equiv., 414). The mother-liquors from the initial crystallization of the lupulone were diluted with methanol (1 l.), the solution set aside for 30 minutes, and the upper layer decanted from black resin. A solution of lead acetate (238 g.) in a mixture of methanol (250 c.c.) and water (140 c.c.) was added, and the precipitate filtered off on kieselguhr (Hyflo Supercel) and washed with methanol. The air-dried humulone lead salt weighed 483 g.

(b) *From lupulin.* A suspension of Horst's Fancy Oregon lupulin (500 g.) in methanol (2 l.) was set aside under nitrogen overnight. The suspension was then filtered and the residue was washed thoroughly with methanol (500 c.c.) by resuspension. To the filtrate was added a solution of lead acetate (157 g.) in a mixture of water (96 c.c.) and methanol (864 c.c.). The humulone lead salt was filtered off, washed with methanol, and dried in air (yield, 217 g.). The filtrate and washings were combined and diluted with light petroleum (2 l.), followed by 1% aqueous sodium chloride (4 l.). The upper layer was removed and the aqueous layer extracted with light petroleum (1 l.). The combined light petroleum extracts were washed with 1% aqueous sodium chloride, dried (Na_2SO_4), and evaporated under nitrogen *in vacuo* at 40°, leaving a dark oil (119 g.). The oil was dissolved in light petroleum (100 c.c.) and the solution set aside at 0° while lupulone (35 g.), m. p. 86—91°, separated. A second crop (9·6 g.) was obtained by concentration of the mother-liquors. The combined crops were recrystallized from 90% aqueous methanol, giving lupulone (45 g.), m. p. 89°.

Lupuloxinic Acid.—To a solution of lupulone (10 g.) in 10% aqueous sodium hydroxide (500 c.c.) at room temperature was added 30% hydrogen peroxide (40 c.c.), and the solution was kept at room temperature for 5 hours. The gel resulting was stirred into iced 10% sulphuric acid (1 l.) and the mixture was cooled to 0° overnight. The *lupuloxinic acid* was filtered off and the filtrate was reserved. The product was dissolved in ethanol (30 c.c.), and treated with water (70 c.c.). When separation was complete, the product was filtered off, dried *in vacuo* over calcium chloride, and thoroughly stirred with light petroleum (b. p. 40—60°) to remove yellow material; *lupuloxinic acid* (5·0 g.), m. p. 107° (decomp.), remained. For analysis the material was recrystallized from aqueous methanol, forming colourless plates, m. p. 107—108° [Found : C, 70·2, 70·6; H, 8·6, 8·4; active H, 0·62%; *M* (Rast), 348; equiv. by titration, 192, 384. $C_{22}H_{32}O_5$ requires C, 70·2; H, 8·5; 2 active H, 0·54%; *M*, 378; equiv. (dibasic acid), 189, 378]. Lupuloxinic acid was soluble, with effervescence, in aqueous sodium hydrogen carbonate, to give a colourless solution. It did not yield a crystalline *p*-bromophenacyl ester under the usual conditions.

The filtrate from the reaction mixture was extracted with ether (5 × 100 c.c.). The combined extracts were shaken with three portions of saturated aqueous sodium hydrogen carbonate, and the aqueous layers were acidified, saturated with sodium chloride, and extracted with ether (5 × 20 c.c.). The combined extracts were dried (Na_2SO_4) and evaporated. The residue was distilled, affording *iso*butyric acid (0·660 g.), b. p. 152—154°, characterized as *p*-bromophenacyl *iso*butyrate, m. p. 76°.

Hydrogenation of Lupuloxinic Acid.—(i) *In the presence of palladium chloride.* Lupuloxinic acid (3·0 g.) in methanol (70 c.c.) containing 5% aqueous palladium chloride (2 c.c.) was shaken with hydrogen. The rapid uptake was of 570 c.c., after which hydrogenation became very slow. The catalyst was filtered off, and the filtrate diluted with water (300 c.c.) and extracted thoroughly with ether. The combined ethereal extracts were washed with water and then extracted thoroughly with saturated aqueous sodium hydrogen carbonate. Acidification of the aqueous layer yielded an oil which soon crystallized. The product was recrystallized from aqueous methanol, affording *hexahydrolupuloxinic acid* (1·38 g.), m. p. 154—164°. By recrystallization from aqueous methanol, a small amount of the pure acid, m. p. 156—157° (decomp.), was obtained (Found: C, 69·3; H, 9·6; active H, 0·63. $C_{22}H_{36}O_5$ requires C, 69·1; H, 9·9; 2 active H, 0·53%). The acid gave no colour with ferric chloride.

The ethereal extracts, having been extracted with sodium hydrogen carbonate, were extracted with 2N-sodium hydroxide (2 × 100 c.c.). The combined sodium hydroxide extracts were acidified with hydrochloric acid, to give a sticky semicrystalline precipitate which, on recrystallization from aqueous methanol, yielded *hexahydrolupulenol* (0·68 g.), m. p. 178° [Found: C, 74·9, 74·9; H, 11·2, 11·2; active H, 0·55%; *M* (Rast), 334; equiv. by titration, 332. $C_{21}H_{36}O_3$ requires C, 74·6; H, 11·3; 2 active H, 0·60%; *M*, 338; equiv. (for monobasic acid), 338]. Hexahydrolupulenol was soluble in 2N-sodium hydroxide, and was not affected by aqueous sodium hydrogen carbonate. Potentiometric titration showed the compound to have p*K* 6·3, and to be monobasic. Heating hexahydrolupulenol in refluxing toluene with phenyl *iso*cyanate for 1 hour gave the *phenylurethane*, in poor yield, as colourless rhombs (from aqueous methanol), m. p. 148° (Found: N, 3·2. $C_{28}H_{43}O_4N$ requires N, 3·1%). The enol (0·5 g.) was recovered unchanged after being heated under reflux with a solution of 12N-hydrochloric acid (1 c.c.) in methanol (20 c.c.).

(ii) *In the presence of platinum oxide.* Lupuloxinic acid (900 mg.) in dioxan (30 c.c.) and glacial acetic acid (20 c.c.) was hydrogenated at 22° in the presence of Adams's platinum oxide. Uptake of hydrogen became very slow after 137 c.c. had been absorbed (theor. for 3 double bonds, 160·5 c.c.). When a further quantity of Adams's catalyst was added, rapid uptake of hydrogen occurred during 5 minutes, after which hydrogenation became very slow. The total uptake was 200 c.c. The catalyst was removed, and the filtrate evaporated. The crystalline residue was recrystallized from aqueous methanol, affording hexahydrolupulenol (506 mg.), m. p. and mixed m. p. 178°.

Lupulenol.—A suspension of lupuloxinic acid (2·0 g.) in toluene (15 c.c.) was heated slowly to boiling. At just over 100°, carbon dioxide was evolved (baryta test). After 5 minutes' refluxing the yellow solution was cooled to 0°, seeded, and stored overnight at 0°. *Lupulenol* (1·7 g.) was filtered off, washed with light petroleum, and dried. The m. p. was 118°, unchanged by crystallization from aqueous methanol (needles) [Found: C, 76·1; H, 9·4; active H, 0·52%; *M* (Rast), 297; equiv. by titration, 337. $C_{21}H_{32}O_3$ requires C, 75·9; H, 9·7; 2 active H, 0·60%; *M*, 332; equiv., 332]. Lupulenol was insoluble in aqueous sodium hydrogen carbonate. It dissolved in 2N-aqueous sodium hydroxide and was precipitated unchanged on acidification. In 50% aqueous methanol the acid had p*K* 6·4. Treating lupulenol (0·2 g.) with 12N-hydrochloric acid (5 c.c.) in methanol (20 c.c.) under reflux gave a yellow solution: the product could not be crystallised.

Hexahydrolupulenol.—Lupulenol (5 g.) in methanol (50 c.c.), hydrogenated over Adams's platinum oxide catalyst, absorbed 104 c.c. of hydrogen (theor. for 3 double bonds, 101 c.c.). The catalyst was removed and the methanol was evaporated *in vacuo*. The residue was crystallized from aqueous methanol, giving hexahydrolupulenol (5 g.), m. p. and mixed m. p. 178°.

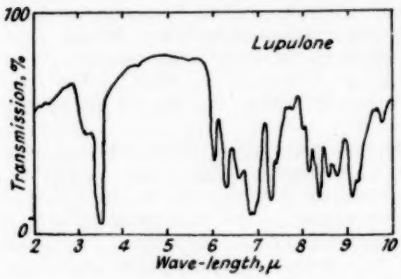
Periodate Oxidation of Lupulenol.—A solution of lupulenol (2·6 g.) in ethanol (65 c.c.) gave a clear solution in aqueous sodium metaperiodate (1·8 g. in 26 c.c.). After 5 seconds sodium iodate began to separate. After 1 hour the sodium iodate (1·4 g.) was filtered off and washed with ethanol. The filtrates were diluted with water (400 c.c.), acidified with 2N-hydrochloric acid (20 c.c.), and extracted with ether (300 and 150 c.c.). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated, to leave a yellow oil. This was treated with 2N-sodium hydroxide (100 c.c.) under reflux for 6 hours. The insoluble material was removed with ether and the ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. The yellow oil which remained was distilled at 196°/40 mm. as a pale yellow oil (0·5 g.). Redistillation at 196°/40 mm. gave a colourless oil, n_D^{12} 1·4832 [Found: C, 82·4; H, 11·7; active H, 0·07%; *M* (Rast), 218. $C_{18}H_{30}O$ requires C, 82·4; H, 11·4%; *M*, 262].

Hydrogenation of the Compound, $C_{18}H_{30}O$.—The compound (1·2 g.), when hydrogenated in

methanol (20 c.c.) over Adams's platinum oxide, absorbed 320 c.c. of hydrogen (theor. for three double bonds, 312 c.c.). The *hexahydro*-derivative, isolated by means of ether, was a colourless oil (1·0 g.), b. p. 166°/20 mm., n_D^{12} 1·4506, d_{12}^{12} 0·845 (Found: C, 80·2; H, 13·3. $C_{18}H_{36}O$ requires C, 80·6; H, 13·5%).

Periodate Oxidation of Hexahydrolupulenol.—Hexahydrolupulenol (4 g.) in ethanol (100 c.c.) was mixed with aqueous sodium metaperiodate (2·7 g. in 40 c.c.). After 1 hour the sodium iodate (2·3 g.) was filtered off and washed with ethanol. The fitrate was worked up in the usual way, to yield a yellow resin which was heated under reflux with 2N-sodium hydroxide for 6 hours. The oil was removed with ether, dried, and isolated. The product was distilled at 168°/20 mm., affording the compound, $C_{18}H_{36}O$ (1·2 g.), n_D^{20} 1·4445, d_{12}^{20} 0·845.

Oxidation of the Compound, $C_{18}H_{36}O$.—The compound (0·8 g.) was heated with refluxing concentrated nitric acid (40 c.c.) for 2 hours. The solution was diluted with water (250 c.c.), saturated with salt, and extracted with ether (3 × 50 c.c.). The combind ethereal extracts were extracted with saturated aqueous sodium hydrogen carbonate (3 × 20 c.c.). The combined extracts were acidified with 12N-hydrochloric acid, saturated with sodium chloride, and extracted with ether (3 × 50 c.c.). The ethereal solutions were dried ($CaCl_2$) and evaporated, leaving an acid which was distilled at *ca.* 166°/760 mm. (80 mg.). The product was converted into the *p*-bromophenacyl ester, which crystallized as plates, m. p. 67°, from methanol. Mixtures with the following *p*-bromophenacyl esters had the m. p.s shown (m. p. of authentic material in parentheses): *iso*butyrate (77°), 54°; *iso*valerate (68°), 57°; 4-methylpentanoate (76°), 73°.



Infra-red Spectra.—The infra-red absorption spectrum of lupulone in Nujol mull (see Fig.) shows a band at 3130 cm.$^{-1}$, ascribed to a hydrogen-bonded OH group. Carbonyl bands occur at 1588 and 1666 cm.$^{-1}$, the former being attributed to a hydrogen-bonded carbonyl group and the latter to a non-bonded, conjugated carbonyl group. A band at 1100 cm.$^{-1}$ cannot be positively identified, although it is not inconsistent with the presence of an ether grouping. The triply substituted C=C group is identified as that giving rise to the band at 827 cm.$^{-1}$.

The authors thank Sir Ian Heilbron, D.S.O., F.R.S., and Dr. A. H. Cook, F.R.S., for helpful advice and encouragement, Dr. N. Sheppard for infra-red spectra, and Dr. E. A. Braude, Dr. T. F. Macrae, and Miss J. M. Fabian for ultra-violet absorption spectra. Microanalyses were carried out by Messrs. Weiler and Strauss, Oxford.

THE BREWING INDUSTRY RESEARCH FOUNDATION,
NUTFIELD, SURREY.

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351. *The Chemistry of Hop Constituents. Part III.* The Structures of Humulinic and* iso*Humulinic Acids.*

By G. HARRIS, G. A. HOWARD, and J. R. A. POLLOCK.

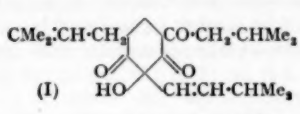
Humulone has been degraded through *iso*humulinic acid to 3-4′-methylbutyl*cyclo*pentane-1 : 2 : 4-trione which has been synthesized. New oxidative degradations of humulinic and dihydrohumulinic acids have been carried out and the structures of these compounds and of humulone are discussed.

ALTHOUGH the hop constituent humulone, $C_{21}H_{30}O_5$, has recently been synthesized by Riedl (*Brauwiss.*, 1951, 85), the method used was equivocal and, moreover, the reactions of the compound are difficult to reconcile with the proposed formulation (I). It is essential for an understanding of these reactions that the structures of the reaction products should be firmly established and the present work was undertaken in an attempt to confirm the structures of humulinic and *iso*humulinic acids, two important degradation products of humulone.

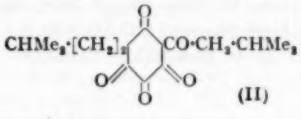
* Part II, preceding paper.

Wöllmer observed (*Ber.*, 1916, **49**, 780) that humulone was very readily reduced in the presence of palladium chloride to a volatile hydrocarbon and humuloquinol, $C_{16}H_{24}O_5$, the latter being readily oxidised by air to the corresponding quinone (II). This reduction, typical of an allyloxy-compound, remains without analogies if humulone has the structure (I) which was assigned to it when Wieland (*Ber.*, 1925, **58**, 102) extended Wöllmer's work on humulone and humuloquinone and degraded the latter to *iso*humulinic acid, $C_{15}H_{22}O_4$, for which the structure (III; R = $CO{\cdot}CH_2{\cdot}CHMe_2$) was postulated. In agreement with this formulation *iso*humulinic acid forms an azine with *o*-phenylenediamine, a dioxime, and a mono-oxime methyl ether. As explained below, however, the conversion of (III) into dihydrohumulinic acid by reduction or of dihydrohumulinic acid into (III) by oxidation could not be effected; these transformations should be possible if *iso*humulinic acid and dihydrohumulinic acid have the structures (III; R = $CO{\cdot}CH_2{\cdot}CHMe_2$) and (IV; R′ = $CH_2{\cdot}CH_2{\cdot}CHMe_2$) respectively ascribed to them by Wieland. A verification of the Wieland structure for *iso*humulinic acid was, therefore, considered desirable.

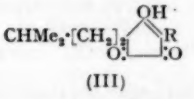
Treatment of the compound with cold alkali gave *iso*valeric acid and a crystalline substance, $C_{10}H_{14}O_3$, which gave a strong colour with methanolic ferric chloride and had p*K* 6·9 in 50% aqueous acetone. This compound formed an azine with *o*-phenylenediamine and, unlike its precursor, readily gave a benzylidene derivative with benzaldehyde; it was thus thought likely that it was 3-3′-methylbutyl*cyclo*pentane-1 : 2 : 4-trione (III; R = H) and its synthesis was effected by the following method (cf. Diels, Sielisch, and Muller, *Ber.*, 1906, **39**, 1328). Two equivalents of ethyl oxalate were condensed with one of 6-methylheptan-2-one in boiling ethanolic sodium ethoxide to give 3-ethoxalyl-



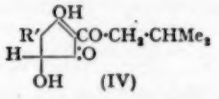
(I)



(II)



(III)



(IV)

5-3′-methylbutyl*cyclo*pentane-1 : 2 : 4-trione which was hydrolysed by aqueous methanolic hydrogen chloride to the required 3-3′-methylbutyl*cyclo*pentane-1 : 2 : 4-trione, identical with the material isolated by hydrolysis of *iso*humulinic acid. There can be no doubt, therefore, that the latter is correctly represented by (III; R = $CO{\cdot}CH_2{\cdot}CHMe_2$). Preliminary attempts to acylate (III; R = H) to (III; R = $CO{\cdot}CH_2{\cdot}CHMe_2$) have been unsuccessful.

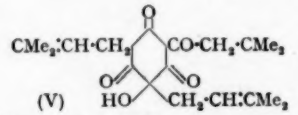
Attention was next turned to the structure of humulinic acid and its dihydro-derivative. The former is readily obtained, together with acetone, *iso*butaldehyde, and an unsaturated acid, by alkaline hydrolysis of humulone (Lintner and Schnell, *Z. ges. Brauwesen*, 1904, **27**, 668; Wieland, *loc. cit.*). The unsaturated acid was incorrectly described by Wieland as 4-methylpent-2-enoic acid * and its correct identification as the 3-enoic acid by Cook and Harris (*J.*, 1950, 1873) requires the Wieland structure (I) for humulone to be modified to (V). The reactions of humulinic acid were investigated by Wieland (*Ber.*, 1925, **58**, 2012) and by Wieland and Martz (*Ber.*, 1926, **59**, 2352) who postulated the structure (IV; R′ = $CH_2{\cdot}CH{:}CMe_2$) for it although the formulation (VI; R′ = $CH_2{\cdot}CH{:}CMe_2$) is equally possible on Wieland's evidence. Since diphenyl*cyclo*pentanetrione (Ruggli and Schmidlin, *Helv. Chim. Acta*, 1946, **29**, 383) and methyl*cyclo*pentanetrione (Orchin and Butz, *J. Amer. Chem. Soc.*, 1943, **65**, 2296) can be hydrogenated to hydroxy*cyclo*pentanediones it was expected that partial hydrogenation of *iso*humulinic acid would lead smoothly to a dihydro-derivative likely to be identical with (IV; R′ = $CH_2{\cdot}CH_2{\cdot}CHMe_2$). Although the course of the hydrogenation of *iso*humulinic acid is not simple the dihydro-derivative isolated was different from dihydrohumulinic acid. This dihydro*iso*humulinic acid should be either (IV; R′ = $CH_2{\cdot}CH_2{\cdot}CHMe_2$) or (VI; R′ = $CH_2{\cdot}CH_2{\cdot}CHMe_2$) since the method of prepar-

* Geneva convention, CO_2H = 1.

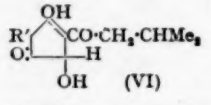
ation could equally well lead to either compound and the properties of dihydrohumulinic acid are as well explained by one structure as by the other.

Since *iso*humulinic acid could not be reduced to dihydrohumulinic acid, oxidation of the latter to the former was investigated. The oxidation of a secondary α-ketol group is normally easy and, if dihydrohumulinic acid is (IV) or (VI), should readily afford *iso*humulinic acid (III; R = $CO{\cdot}CH_2{\cdot}CHMe_2$). Fehling's solution unexpectedly failed to affect either humulinic or dihydrohumulinic acid. In view of the stability of *iso*humulinic acid to hypobromite (Wieland, *loc. cit.*) the action of this reagent on humulinic acid was investigated. Both this acid and its dihydro-derivative readily reduce three equivalents of hypobromite but the cyclic structure is destroyed, bromoform and *iso*valeric acid being formed in both cases. With dihydrohumulinic acid, a crystalline acid, $C_9H_{16}O_5$, was also obtained. This compound behaved as an α-hydroxy-acid and may well be the 1-hydroxy-5-methylhexane-1 : 2-dicarboxylic acid (VII) expected if dihydrohumulinic acid has the structure (IV; R′ = $CH_2{\cdot}CH_2{\cdot}CHMe_2$). The oxidation of cyclic β-diketones with hypohalites is well known (cf. Ingold and Thorpe, *J.*, 1922, 157) but the ready oxidations of humulinic and dihydrohumulinic acids are in strong contrast to the stability of *iso*humulinic acid to hypobromite.

Humulinic acid readily reduces one equivalent of periodate with evolution of carbon dioxide and the formation of an enolic compound which is hydrolysed by alkali to *iso*valeric acid and 5-methylhex-4-enoic acid, together with *iso*butyl methyl ketone and 6-methylhept-5-en-2-one. A compound with structure (IV; R′ = $CH_2{\cdot}CH{:}CMe_2$) would reduce one equivalent of periodate and give the di-β-keto-carboxylic acid (VIII). Decarboxylation of this would lead to 2-(3-keto-5-methylhexanoyl)-5-methylhex-4-enal (VIII, with H in place of CO_2H) which would then be further hydrolysed by alkali to the products actually isolated. Although the results of the periodate and hypobromite



(V)



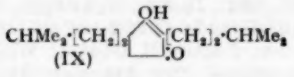
(VI)

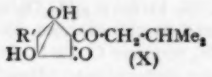
$CHMe_2{\cdot}[CH_2]_2{\cdot}CH(CO_2H){\cdot}CO_2H$ (VII)

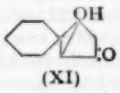
$CMe_2{:}CH{\cdot}CH_2{\cdot}CH(CHO){\cdot}CO{\cdot}CH(CO_2H){\cdot}CO{\cdot}CH_2{\cdot}CHMe_2$ (VIII)

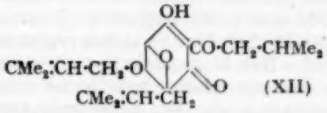
oxidation of humulinic acid are explicable on the basis of (IV; R′ = $CH_2{\cdot}CH{:}CMe_2$), this structure still leaves unexplained its stability towards Fehling's solution and also to alkali and acid. Equally inexplicable is the ready reduction of both humulinic and dihydrohumulinic acids to hydrocarbons by the Clemmensen procedure (Wieland and Martz, *loc. cit.*). In the case of dihydrohumulinic acid an intermediate deoxy-compound was obtained and ascribed by Wieland and Martz the structure (IX). The stability of the deoxy-compound to both acid and alkaline hydrolysis, coupled with the absence of ketonic reactions and of coloration with methanolic ferric chloride, are, however, inconsistent with this formulation. Present results, in fact, support a formula, $C_{14}H_{24}O_2$, rather than $C_{15}H_{26}O_2$ as required by (IX). Other properties of humulinic and dihydrohumulinic acid are also difficult to reconcile with formulations such as (IV); *e.g.*, their ultra-violet absorption spectra are quite unlike those of hydroxy*cyclo*pentanediones (Bastron, Davis, and Butz, *J. Org. Chem.*, 1943, **8**, 215). Further they resist hydrolysis by acid or alkali, are even stronger acids (p*K* 3·2 and 3·8 in 50% aqueous acetone) than the *cyclo*pentanetriones (p*K* 4—5 and showing one active H), and yet contain only one of the two active hydrogen atoms to be expected from the formulations (IV). They also fail to give derivatives characteristic of secondary alcohols. These properties, incompatible with (IV), find a ready explanation on the basis of the structure (X; R′ = $CH_2{\cdot}CH{:}CMe_2$ and $CH_2{\cdot}CH_2{\cdot}CHMe_2$) for humulinic and dihydrohumulinic acids respectively. Periodate oxidation of such compounds would lead to hydroxy*cyclo*propanones which would rearrange readily to (VIII). Furthermore, the general properties and hypobromite oxidation of (XI) described by Ingold, Seeley, and Thorpe (*J.*, 1923, 860) are closely analogous to the behaviour observed with humulinic acid. The synthesis of model compounds is being investigated.

Finally, it is pertinent to place on record further experiments designed to test the validity of structure (V) for humulone. A compound with structure (V) would give 4-methylpent-3-enoic acid when oxidised by periodate. While humulone is oxidised by this reagent the formation of 4-methylpent-3-enoic acid does not occur. Again, the fact that


(IX)


(X)


(XI)


(XII)

humulone undergoes hydrogenolysis in the presence of palladium chloride is incompatible with its having the structure (V). It is now suggested that the above difficulties find accommodation in formula (XII). In agreement with this structure it has been ascertained that humulone forms only a monophenylurethane and is a monobasic compound with one active hydrogen atom. The formation of humulinic and 4-methylpent-3-enoic acids from humulone is then readily explained by an allylic rearrangement of (XII), followed by hydrolytic fission of the product.

Experimental

Microanalyses are by Drs. Weiler and Strauss. M. p.s are uncorrected.

Humulone.—To humulone (Wöllmer, *Ber.*, 1916, **49**, 780) (23·1 g.) in acetic acid (440 c.c.), ice-cold water (500 c.c.) was added slowly at 0° with scratching and stirring, to give pale yellow rhombs, m. p. 63° (Found: C, 69·7; H, 8·4; active H, 0·78%; equiv., 379; I.V., 95·5. Calc. for $C_{21}H_{30}O_5$: C, 69·6; H, 8·3; 3 active H, 0·83%; equiv., 362; IV., 70). Ultra-violet absorption: Max., in basic ethanol, 324, 228, and 350—361 shoulder mμ (ε = 11,520, 14,730 and 8750 respectively); in acidic ethanol, 235, 281·5, and 310—325 (shoulder) mμ (ε = 10,100, 8000, and 5330 respectively). The *o*-phenylenediamine complex had m. p. 117—118·5° (Found: C, 69·0; H, 8·3; N, 5·9. Calc. for $C_{27}H_{38}O_5N_2$: C, 68·9; H, 8·1; N, 6·0%). Ultra-violet absorption in ethanol: Max., 230, 242, 280, 330, and 360 mμ (ε = 8500, 5700 5700, and 4300 respectively).

Humulone had p*K* 4·5 in 50% acetone and reduced 1·97 equivs. of periodate producing 3·3 equivs. of acid but none of the expected 4-methylpent-3-enoic acid; it also reduced 4·95 equivs. of perbenzoic acid and absorbed 2·1 equivs. of bromine from a chloroform solution, hydrogen bromide being liberated.

A solution of humulone (500 mg.) and phenyl *iso*cyanate (550 mg.) in light petroleum (b. p. 80—100°) (12 c.c.) was boiled under reflux for 90 minutes under nitrogen, concentrated, and kept overnight at 0°. The product (90 mg.), m. p. 161° (decomp.), was twice recrystallized from light petroleum, giving *humulone phenylurethane*, m. p. 161° (decomp.) (Found: C, 70·0; H, 7·4; N, 3·3. $C_{28}H_{35}O_6N$ requires C, 69·9; H, 7·3; N, 2·9%), which gave a strong red to purple colour with alcoholic ferric chloride.

Humuloquinol.—When prepared by Wöllmer's method (*loc. cit.*), the quinol, was obtained as yellow granules, m. p. 126—128°, giving a red colour with alcoholic ferric chloride solution (Found: C, 64·3; H, 8·0; active H, 0·68. Calc. for $C_{14}H_{24}O_5$: C, 64·8; H, 8·2; 2 active H, 0·68%). Ultra-violet absorption: Max.: 293 and 350 mμ (ε = 22,000 and 2400 respectively). *Humuloquinol dimethyl ether*, prepared by an excess of diazomethane in ether, had b. p. 100—115°/10^{-5} mm. (Found: C, 67·1; H, 8·7; OMe, 19·9; active H, 0·25. $C_{18}H_{28}O_5$ requires C, 66·7; H, 8·7; OMe, 19·2; 1 active H, 0·31%), gave a green colour with alcoholic ferric chloride, and failed to form a 2 : 4-dinitrophenylhydrazone.

The *phenylurethane*, prepared in the usual way and recrystallized from benzene–light petroleum (b. p. 60—80°), had m. p. 131° (decomp.) (Found: C, 67·4; H, 7·0; N, 3·4; active H, 0·50. $C_{29}H_{29}O_6N$ requires C, 66·5; H, 7·0; N, 3·4; 2 active H, 0·49%). Benzoylation of humuloquinol in cold pyridine under nitrogen and recrystallizing the product from ethanol gave humuloquinol tetrabenzoate, m. p. 167° (Found: C, 73·6; H, 5·9; active H, 0·0. Calc. for $C_{44}H_{40}O_9$: C, 73·7; H, 5·6%). Ultra-violet absorption: Max., 234 mμ (ε = 72,000).

Humuloquinone.—Humuloquinone, prepared by Wöllmer's method (*loc. cit.*), had m. p. 84° after recrystallization from methanol (Found: C, 65·5; H, 7·5; active H, 0·73. Calc. for $C_{16}H_{22}O_5$: C, 65·3; H, 7·5; 2 active H, 0·66%). Ultra-violet absorption: Max., 292 and 510 mμ (ε = 29,000 and 1000 respectively). Treatment with Brady's reagent gave *humuloquinone* 2 : 4-*dinitrophenylhydrazone*, m. p. 215°, as violet laths (from acetic acid) (Found: C, 55·2; H, 5·7; N, 11·4. $C_{22}H_{26}O_8N_4$ requires C, 55·7; H, 5·5; N, 11·8%). Humuloquinone azine, recrystallized from methanol, had m. p. 110° (Found: C, 72·2; H, 7·2; N, 7·5; active H 0·44. $C_{32}H_{26}O_3N_2$ requires C, 72·1; H, 7·2; N, 7·6; 2 active H, 0·54%); Wöllmer gives m. p. 109°. Ultra-violet absorption: Max., in basic ethanol, 299, 344, and 218—220 (shoulder) mμ (ε = 17,000, 10,200, and 10,600 respectively); in acidic ethanol, 292 and 381 mμ (ε = 25,500 and 725 respectively); the band in the visible region is at 530 mμ with ε = 268.

iso*Humulinic Acid.*—Humuloquinone (1·4 g.) was dissolved in cold freshly boiled 2N-sodium hydroxide (300 c.c.), and the solution kept under nitrogen for 2 hours and acidified at 0° with concentrated hydrochloric acid. The acids were extracted with ether, and the extract was washed with water, dried, and evaporated under nitrogen. The residue was crystallized from methanol, giving *iso*humulinic acid (465 mg., 37%), m. p. 141°. Recrystallization gave pure material, m. p. 144° (Found: C, 67·7; H, 8·4; active H, 0·30. Calc. for $C_{15}H_{22}O_4$: C, 67·6; H, 8·3; 1 active H, 0·38%). The compound did not depress the m. p. (143°) of the *iso*humulinic acid prepared by Wieland's method (*loc. cit.*). Ultra-violet absorption: Max., 251, 258 (double peak), and 280 mμ (ε = 25,000 and 22,000 respectively).

To a solution of diazomethane (0·002 mole) in dry ether (40 c.c.) was added *iso*humulinic acid (0·266 g., 0·001 mole). After 10 minutes at room temperature the ether was distilled off leaving a residue which could not be crystallized. Conversion into the oxime in the usual way gave iso*humulinic acid methyl ether oxime*; recrystallized from ether–light petroleum (b. p. 40—60°), it had m. p. 100° (Found: C, 65·0; H, 8·4; N, 4·6. $C_{16}H_{25}O_4N$ requires C, 65·1; H, 8·6; N, 4·8%).

*iso*Humulinic acid (0·133 g.) was refluxed in aqueous methanol (10 c.c.) with hydroxylamine hydrochloride (0·1 g.) and anhydrous sodium acetate (0·15 g.) for 10 minutes. Dilution with water (20 c.c.) and cooling gave the crude *dioxime*, m. p. 202° (decomp.). Recrystallized from aqueous dioxan, this had m. p. 205° (decomp.) (Found: C, 61·4; H, 7·8; N, 9·5. $C_{15}H_{24}O_4N_2$ requires C, 60·8; H, 8·1; N, 9·5%).

Hydrogenation of iso*Humulinic Acid.*—*iso*Humulinic acid (670 mg.) in methanol (30 c.c.) in the presence of Adams's platinum oxide slowly absorbed 160 c.c. of hydrogen overnight. The filtered solution was evaporated and extracted with boiling light petroleum (10 c.c.). Insoluble material (99 mg.), m. p. 160°, was filtered off, and the filtrate concentrated to small bulk and allowed to crystallize at 0°. A pale yellow *dihydro-acid* (140 mg.), m. p. 81°, separated and was filtered off. Recrystallized from light petroleum it had m. p. 88° (Found: C, 67·2; H, 8·8. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%). Ultra-violet absorption: Max., 250 mμ (ε = 15,000).

Alkaline Hydrolysis of iso*Humulinic Acid.*—A solution of *iso*humulinic acid (1 g.) in freshly boiled 2N-sodium hydroxide (60 c.c.) was steam-distilled for 45 minutes. The residue was acidified at 0° and then set aside in a refrigerator. Crystalline material, m. p. 98°, separated and was filtered off. The filtrate was extracted with ether and the bicarbonate-soluble portion obtained from this extract was cooled to −80° in light petroleum. Material, m. p. 95°, separated and was combined with the compound, m. p. 98°, whose m. p. it did not depress. The filtrate from the low-temperature crystallization was evaporated, to give 173 mg. of an acid. This acid gave only one band on a buffered silica column in 1% butanol–chloroform (cf. Moyle, Baldwin, and Scarisbrick, *Biochem. J.*, 1948, **43**, 308) and was converted through the acid chloride into *iso*valeranilide, m. p. and mixed m. p. 110° (Found: C, 74·2; H, 8·4. Calc. for $C_{11}H_{15}ON$: C, 74·6; H, 8·5%). The combined crops of crystalline material of m. p. 95 and 98° were recrystallized from light petroleum (b. p. 40—60°), giving 3-3′-*methylbutyl*cyclo*pentane*-1 : 2 : 4-*trione* (21 mg.), m. p. 102° (Found: C, 66·2; H, 7·9. $C_{10}H_{14}O_3$ requires C, 66·0; H, 7·7%).

With *o*-phenylenediamine in hot methanol the trione gave a yellow azine (77%), m. p. 210° (decomp.).

3-*Ethoxalyl*-5-3′-*methylbutyl*cyclo*pentane*-1 : 2 : 4-*trione.*—A mixture of ethyl oxalate (11 g.) and 6-methylheptan-2-one (10 g.) was added to a solution of sodium (1·8 g.) in dry ethanol (40 c.c.), cooled in ice. A solution of ethyl oxalate (11 g.) in a sodium ethoxide solution, prepared from sodium (1·8 g.) and dry ethanol (40 c.c.), was then added and the mixture heated under reflux for 15 minutes. The hot mixture was saturated with dry hydrogen chloride, cooled, and filtered. The deposited sodium chloride was washed with dry ethanol and the combined filtrates and washings were evaporated *in vacuo*. The residue was dissolved in ethyl acetate and ether,

and the solution extracted with saturated sodium hydrogen carbonate solution. The extracts were acidified and the acids extracted with ether. The ethereal extract was washed, dried, and evaporated to give the ethoxalyl-trione (9 g., 40%), m. p. 74°. This could not be purified for analysis but treatments with Brady's reagent and methanolic *o*-phenylenediamine gave respectively a 2 : 4-*dinitrophenylhydrazone* as yellow plates, m. p. 156° (Found : C, 51·9; H, 4·6; N, 12·4. $C_{20}H_{22}O_9N_4$ requires C, 52·0; H, 4·8; N, 12·1%), and an *azine* as a deep red powder, m. p. 284° (decomp.) (Found : C, 66·8; H, 5·4; N, 8·6. $C_{18}H_{16}O_4N_2$ requires C, 66·3; H, 5·6; N, 8·4%).

3-3′-*Methylbutyl*cyclo*pentane*-1 : 2 : 4-*trione*.—A solution of the foregoing ethoxalyl-trione (9 g.) in methanol (200 c.c.) and 12N-hydrochloric acid (200 c.c.) was refluxed for 3 hours until evolution of gas ceased. The solution was concentrated to half its bulk in a vacuum and then set aside in a refrigerator. The product (6 g.) was filtered off and a further crop (1 g.) was obtained by concentration of the mother liquors. The combined crops were recrystallized from benzene and light petroleum, giving 3-3′-methylbutyl*cyclo*pentane-1 : 2 : 4-trione (4 g., 69%), m. p. 102° undepressed by admixture with a specimen prepared from *iso*humulinic acid (Found : C, 65·7; H, 7·8%). The 2 : 4-*dinitrophenylosazone* crystallized in scarlet needles, m. p. 228° (decomp.), from ethyl acetate (Found : C, 48·6; H, 3·6; N, 20·5. $C_{22}H_{20}O_9N_8$ requires C, 48·9; H, 3·7; N, 20·7%). The *benzylidene* derivative, m. p. 216°, crystallized from aqueous methanol (Found : C, 75·0; H, 6·6. $C_{17}H_{16}O_3$ requires C, 75·6; H, 6·7%). The *azine* had m. p. 230° (decomp.) (Found : C, 75·8; H, 7·4; N, 10·7. $C_{16}H_{18}ON_2$ requires C, 75·6; H, 7·1; N, 11·2%). Ultra-violet absorption : Max., in acidic ethanol, 275·5 mμ (ε = 12,230); in basic ethanol, 326 and 233·5 mμ (ε = 10,800 and 10,500 respectively).

Humulinic Acid.—The compound, prepared by Wöllmer's method (*loc. cit.*) and recrystallized from *cyclo*hexane (68% yield), had m. p. 93° (Found : C, 67·4; H, 8·4; active H, 0·3%; equiv., 278. Calc. for $C_{15}H_{22}O_4$: C, 67·6; H, 8·3; 1 active H, 0·38%; equiv., 266). Ultra-violet absorption : Max., in acidic ethanol, 266 and 225·5 mμ (ε = 9620 and 9630 respectively); in basic ethanol, 250 and 262·5—269 mμ (shoulder) (ε = 20,600 and 16,420 respectively). Wöllmer (*loc. cit.*) gives m. p. 92°.

Humulinic acid decolourised bromine in chloroform, gave a red colour with alcoholic ferric chloride solution, and was soluble in sodium hydrogen carbonate solution. It did not reduce hot Fehling's solution, failed to form an azine with *o*-phenylenediamine, and was recovered unchanged in excellent yield when boiled under reflux for 3 hours with methanolic hydrochloric acid (5 vols. of methanol with 2 vols. of concentrated hydrochloric acid). Humulinic acid was stable indefinitely to boiling 2N-sodium hydroxide. It reduced a total of 0·8 equiv. of periodate with the formation of 1·8 equivs. of acid. With excess of lithium aluminium hydride in boiling ether it gave a neutral oil which gave no colour with alcoholic ferric chloride and gave a resinous urethane and an oily dark red 2 : 4-dinitrophenylhydrazone.

The oxime was prepared in aqueous solution in the usual way, the crude product being extracted with boiling ether and recrystallized from methanol; it had m. p. 150° (Found : C, 63·5; H, 7·9; N, 5·1. Calc. for $C_{15}H_{23}O_4N$: C, 64·0; H, 8·2; N, 5·0%). Wieland (*loc. cit.*) gives m. p. 152—153°. The ultra-violet absorption spectrum in ethanol was very similar to that of dihydrohumulinic acid oxime : Max., 251 and 303; Min., 272 mμ (ε = 16,700, 18,000, and 6800 respectively).

Hypobromite Oxidation of Humulinic Acid.—To a cold solution of humulinic acid (5 g.) in N-sodium hydroxide (200 c.c.) was slowly added, dropwise with shaking, a saturated aqueous solution of bromine (300 c.c.) until a slight excess of hypobromite was present. The solution was extracted with ether, and the ethereal extract washed with water, dried, and evaporated, to give bromoform (b. p. 149°; 2·6 g., 55%). The alkaline oxidised solution was acidified and extracted with ether. The ethereal extract was washed with water and then extracted with saturated aqueous sodium hydrogen carbonate solution. The alkaline extract was acidified, the acids were extracted with ether, and the ethereal extract washed with water, dried, and evaporated, giving an oil which was extracted with boiling light petroleum. The petroleum solution, on evaporation, gave *iso*valeric acid (0·94 g., 50%) (*p*-bromophenacyl ester, m. p. 67°, undepressed by admixture with an authentic specimen).

Periodate Oxidation of Humulinic Acid.—(*a*) To a solution of humulinic acid (5·02 g.) in ethanol (80 c.c.) was added one of sodium metaperiodate (4·4 g.) in water (80 c.c.). After 5 minutes sodium iodate began to separate and carbon dioxide was evolved (baryta test). After 6 hours the sodium iodate (3·7 g., 90%) was filtered off and washed with a little ethanol. The combined filtrate and washings were diluted with water and extracted with ether. The aqueous solution was made slightly acid, saturated with sodium chloride, and extracted with ether. The

combined ethereal extracts were washed with water, dried, and evaporated. The oily residue was dissolved in 2N-sodium hydroxide (100 c.c.) and the solution refluxed for 2 hours. The cooled solution was extracted with ether and the extract washed with water, dried, and evaporated, to give the ketonic fraction. The alkaline solution was acidified and extracted with ether; the bicarbonate-soluble fraction from this extract was converted into *p*-bromophenacyl 5-methylhex-4-enoate, m. p. 83° (from ethanol) undepressed by admixture with a specimen prepared from the authentic acid (Staudinger, *Helv. Chim. Acta*, 1922, **5**, 751) [Found: C, 54·6; H, 5·2%; *M* (Rast), 314. $C_{15}H_{17}O_3Br$ requires C, 55·2; H, 5·5%; *M*, 326]. The ketonic fraction was distilled, to give a fraction, b. p. 80—83°, and a residue. The distillate gave a 2 : 4-dinitrophenylhydrazone, m. p. 83° (Found: C, 51·6; H, 5·7; N, 19·7. Calc. for $C_{12}H_{16}O_4N_4$: C, 51·4; H, 5·7; N, 20·0%), undepressed by admixture with the 2 : 4-dinitrophenylhydrazone of *iso*butyl methyl ketone. The residual ketone was converted into a 2 : 4-dinitrophenylhydrazone, m. p. 87°, undepressed by admixture with that of authentic 6-methylhept-5-en-2-one prepared from citral (Verley, *Bull. Soc. chim.*, 1897, **17**, 176).

(*b*) In another experiment, with humulinic acid (17 g.), the oily oxidation product was divided into neutral (2·4 g.), bicarbonate-soluble (1·1 g.), and caustic-soluble (9·5 g.) fractions in the usual way. No recognisable products were obtained from the neutral and acidic fractions. The enolic fraction was hydrolysed in boiling 2N-sodium hydroxide (50 c.c.) under reflux for 3 hours and then divided into neutral (4·7 g.), acidic (1·85 g.), and enolic (0·38 g.) fractions in the usual way. The acidic fraction was distilled, to give only *iso*valeric acid, b. p. 166° (Found: equiv., 99·4. Calc. for $C_4H_9{\cdot}CO_2H$: equiv., 102) (*p*-bromophenacyl ester, m. p. 67° undepressed by admixture with an authentic specimen). The neutral fraction from the hydrolysis was distilled and the fraction, b. p. 106° (0·3 g.), collected. Higher-boiling fractions gave no recognisable derivatives. The fraction, b. p. 106°, gave a 2 : 4-dinitrophenylhydrazone, m. p. 87°, undepressed by admixture with that of authentic 6-methylhept-5-en-2-one (Found: C, 54·6, H, 5·8; N, 18·3. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9; N, 18·3%). A portion of the material, b. p. 106°, was hydrogenated in methanol by use of Adams's platinum oxide; the product gave a 2 : 4-dinitrophenylhydrazone, m. p. 78°, undepressed by admixture with an authentic specimen of 6-methylheptan-2-one 2 : 4-dinitrophenylhydrazone.

Dihydrohumulinic Acid.—Humulinic acid (8·5 g.) in methanol (300 c.c.) in the presence of Adams's platinum oxide absorbed 700 c.c. of hydrogen in 2 hours. The solution was concentrated and the product allowed to crystallize. Recrystallization from ethanol and then from *cyclo*hexane gave dihydrohumulinic acid (7·6 g., 90%), m. p. 126° (Found: C, 66·8; H, 8·9; active H, 0·40%; equiv., 268. Calc. for $C_{15}H_{24}O_4$: C, 67·2; H, 9·0; 1 active H, 0·37%; equiv., 268). Wöllmer (*loc. cit.*) gives m. p. 125—126°. Ultra-violet absorption spectrum in ethanol: Max., 259 and 267 mμ (ε = 9500 and 10,500 respectively). Dihydrohumulinic acid was soluble in sodium hydrogen carbonate solution and gave a yellow colour with alcoholic ferric chloride. It failed to reduce Fehling's solution or ammoniacal silver nitrate and was recovered unchanged after attempts to prepare its phenylurethane or to oxidise it with alkaline hydrogen peroxide. Dihydrohumulinic acid consumed 0·98 equiv. of periodate with the formation of 1·94 equivs. of acid.

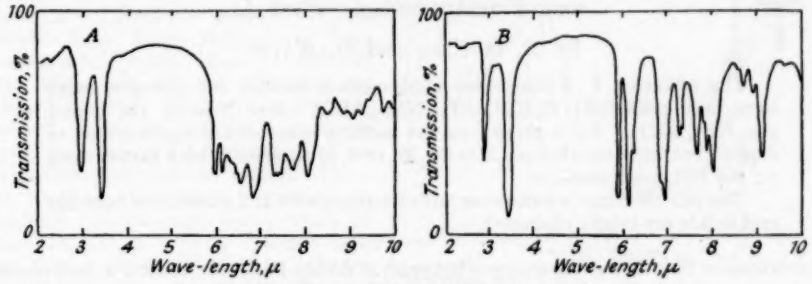
The *oxime*, prepared in the usual way and recrystallized from methanol and from ether–*cyclo*hexane, had m. p. 125° (Found: C, 63·6; H, 8·6; N, 5·0. Calc. for $C_{15}H_{25}O_4N$: C, 63·6; H, 8·8; N, 5·0%). The ultra-violet absorption spectrum in ethanol was very similar to that of humulinic acid oxime: Max., 251 and 303; Min., 272 mμ (ε = 16,400, 17,200, and 6700 respectively).

Hydrobromite Oxidation of Dihydrohumulinic Acid.—(*a*) To a cooled solution of dihydrohumulinic acid (2·5 g.) in N-sodium hydroxide (100 c.c.) was added, dropwise, with shaking, a freshly saturated solution of bromine in water (330 c.c.). Excess of bromine was removed by sodium hydrogen sulphite. The solution was extracted with ether; evaporation of the washed dried extract gave bromoform, b. p. 146° (0·928 g., 44%), which gave phenyl *iso*cyanide with aniline and aqueous sodium hydroxide. The alkaline reaction mixture was acidified and the acids extracted with ether. The washed and dried extract was evaporated and distilled, giving *iso*valeric acid, b. p. 160° (0·52 g., 59%), which gave a *p*-bromophenacyl ester, m. p. 68°, undepressed by admixture with an authentic specimen.

(*b*) In another experiment dihydrohumulinic acid (5 g.) absorbed the equivalent of 6 atoms of bromine. The bromoform was removed by light petroleum, and the aqueous alkaline solution acidified and then extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and evaporated, to give a residue (5 g.) which was diluted with light petroleum (50 c.c.) and kept at 0°. A sticky solid, m. p. 94—100° (0·162 g.), separated and was filtered off.

A further crop was obtained by evaporation of the mother-liquors *in vacuo*, dissolution of the residue in benzene (5 c.c.), addition of light petroleum to incipient turbidity, and cooling. The combined crops were boiled with benzene (2 c.c.) to remove oil, and the insoluble material (m. p. 122°; 76 mg.) was filtered off and recrystallized by dissolution in acetone (3 drops) and addition of light petroleum. The product (49 mg.) had m. p. 124° (Found: C, 52·9; H, 7·8; active H, 0·73. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8; 2 active H, 0·98%). The compound was acid to litmus, effervesced with sodium hydrogen carbonate, and evolved carbon monoxide and sulphur dioxide when treated with concentrated sulphuric acid.

Clemmensen Reduction of Dihydrohumulinic Acid.—To a solution of dihydrohumulinic acid (4·2 g.) in a mixture of ethanol (50 c.c.) and concentrated hydrochloric acid (10 c.c.) was added zinc amalgam (20 g.; cf. Fieser *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3203). Dry hydrogen chloride was passed into the mixture for 10 minutes; the solution then no longer gave a colour with ferric chloride after neutralization with sodium hydrogen carbonate. The reaction mixture was diluted with water and extracted with ether. The ethereal solution was washed with water and extracted with saturated aqueous sodium hydrogen carbonate solution, then with 2N-sodium hydroxide, and finally washed with water and dried. Evaporation gave a mixture of high-boiling ketones. Neither these ketones nor their 2 : 4-dinitrophenylhydrazones have been studied further. The sodium hydroxide extract was acidified and extracted with ether. The ethereal extract was washed with water, dried, and evaporated, to give a colourless solid, m. p. 138°. Recrystallization from 70% aqueous methanol gave deoxydihydrohumulinic acid (2·1 g., 60%), m. p. 141° (Found: C, 74·9, 74·9; H, 11·1, 10·9%; equiv., 222. Calc. for



A, Humulone. B, Dihydrohumulinic acid.

$C_{15}H_{24}O_2$: C, 75·7; H, 10·9%; equiv., 238. Calc. for $C_{14}H_{24}O_2$: C, 75·7; H, 10·7%; equiv., 224). Wieland and Martz (*loc. cit.*) give m. p. 146°. Deoxydihydrohumulinic acid did not form a 2 : 4-dinitrophenylhydrazone or an azine with *o*-phenylenediamine. It had p*K* 6·9 in 50% aqueous acetone. The compound was insoluble in aqueous sodium hydrogen carbonate solution, did not give a colour with alcoholic ferric chloride solution, and decolourised a solution of bromine in carbon tetrachloride. Deoxydihydrohumulinic acid was completely stable to Fehling's solution, ammoniacal silver nitrate, alkaline hydrogen peroxide, boiling 10N-sodium hydroxide, and boiling ethanolic hydrochloric acid (3 vols. of ethanol to 2 of concentrated hydrochloric acid). It failed to form a benzylidene derivative with alkaline benzaldehyde, unchanged starting material being recovered; it was not hydrogenated in ethanol in the presence of Adams's platinum oxide and was stable to periodate. The compound reduced aqueous alkaline permanganate solution and was oxidised by hypobromite. Dihydrohumulinic acid was recovered unchanged after treatment with gaseous hydrogen chloride for 3 hours in an ethanol solution containing hydrochloric acid, zinc chloride, and mercuric chloride.

Attempted Clemmensen Reduction of 3 : 5-*Diphenylcyclopentane*-1 : 2 : 4-*trione.*—To a solution of this trione (2 g.) (Claisen, *Annalen*, 1895, **284**, 250) in ethanol (50 c.c.) and concentrated hydrochloric acid (20 c.c.) was added zinc amalgam (20 g.), and dry hydrogen chloride was passed into the mixture rapidly for 3 hours. The reaction mixture was then worked up as in the dihydrohumulinic acid reduction. The portion soluble in sodium hydroxide solution gave unchanged starting material (1·9 g.), m. p. and mixed m. p. 193°.

Infra-red Spectra.—The infra-red spectra of humulone and dihydrohumulinic acids are compatible with the structures suggested (see Fig.).

The spectrum of humulone in Nujol mull showed a band at 3300 cm.$^{-1}$ attributed to a non-hydrogen-bonded hydroxyl. The asymmetry of this peak suggests that a hydrogen-bonded

enolic hydroxyl group is also present in the molecule. Carbonyl bands are present at 1626 and 1663 cm.$^{-1}$, the latter being due, probably to a conjugated carbonyl group and the former to a group which is hydrogen-bonded so as to form a six-membered ring. The band at 836 cm.$^{-1}$ is typical of a triply substituted C=C group. This evidence is consistent with the enolic forms of (V) or (XII) containing internal hydrogen bonding. The spectrum is very similar in its essentials to that of lupulone (preceding paper).

The infra-red spectrum of dihydrohumulinic acid shows a very sharp hydroxyl band at 3420 cm.$^{-1}$; the slight asymmetry of the band suggests the presence of a hydrogen-bonded hydroxyl group. The carbonyl bands at 1690 and 1629 cm.$^{-1}$ are attributed to one hydrogen-bonded and one unbonded group; the dimethyl doublet at 1365 cm.$^{-1}$ is very marked. These data are consistent with structures like (IV) or (X); the sharpness of the hydroxyl band is noteworthy.

We are indebted to Professor A. R. Todd, F.R.S., and Dr. N. Sheppard for the infra-red spectra.

THE BREWING INDUSTRY RESEARCH FOUNDATION,
NUTFIELD, SURREY.

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352. *Aluminium Halide Complexes with Pyridine, Trimethylamine, and Triethylamine. Part I.*

By D. D. ELEY and H. WATTS.

The following 1 : 1 complexes of aluminium halides and nitrogen bases have been prepared: C_5H_5N,AlX_3, NMe_3,AlX_3, where X = Cl, Br, I, and also $NEt_3,AlCl_3$. For a given base the melting point of a complex seems to depend but little on whether X is Cl, Br, or I, in agreement with earlier work on the NH_3 complexes.

The side reactions which occur with triethylamine and aluminium bromide and iodide are briefly discussed.

THE co-ordinate link $R\rightarrow AlX_3$ formed between a donor molecule R and a half-molecule of aluminium halide is of great interest for the theory of Friedel–Crafts catalysis. Previous work from this laboratory has been concerned to estimate the strength of this link in a number of cases by measurements of the heat of mixing of the two components in the presence of an inert diluent (Dilke and Eley, *J.*, 1949, 2601; Dilke, Eley, and Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 261). We now propose a more direct approach to the bond energy through the heat of hydrolysis of the complex, and for this purpose have investigated the preparation of the crystalline 1 : 1 complexes. In this paper we describe the method finally adopted, and its successful application in seven instances. The tertiary amines have been chosen as donor molecules because of the known tendency of primary and secondary amines and ethers to give side reactions.

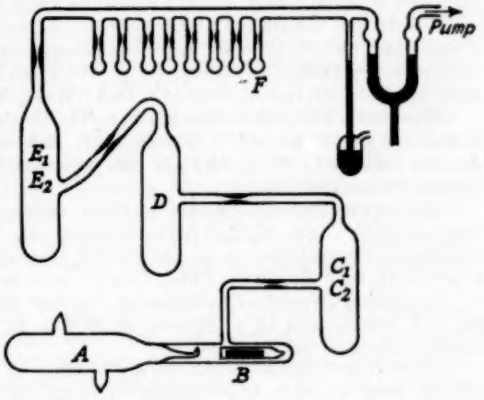
EXPERIMENTAL

Preparative Method.—In accordance with earlier work (*e.g.*, Muller and Bauer, *Z. anorg. Chem.*, 1926, **156**, 69), we found that complexes crystallised from solution contained many molecules of the donor molecule, and sometimes solvent molecules, and were often of indefinite composition. Being primarily interested in 1 : 1 complexes, we finally evolved the following method, which we describe for the specific case of pyridine and aluminium chloride. The preparation throughout was conducted in an all-glass apparatus (see fig.), capable of evacuation to 10^{-6} mm. of Hg, mercury cut-offs being used in place of greased taps wherever necessary. Tube *A* contained pure aluminium chloride which, after the seal had been broken with the magnetic hammer *B* enclosed in glass, was sublimed successively through tubes C_1 and C_2 (only one shown in the diagram), and a third time into the reaction vessel *D*, where it formed a film on the walls of the vessel. After each sublimation the residue-vessel was sealed off and removed. The reaction tube *D* was then cooled in ice and the necessary amount of pyridine condensed into it, from a storage bulb beyond the mercury cut-off and not shown in the diagram.

After ½ hour's contact with the aluminium chloride, excess of pyridine was distilled back into its storage vessel by cooling the latter in liquid oxygen. The complex was then connected to the pumps and heated to near its b. p., until, on raising the cut-off, no increase in pressure occurred. At this stage the complex was distilled twice through vessels E_1 and E_2 (only one shown), and finally sealed off in ampoules *F*, of a size suitable for subsequent calorimetric and dipole work.

Additional Measurements.—M. p.s of the complexes were all determined in the sealed ampoule and are "corrected." The aluminium chloride–pyridine complex was further investigated: the pressure–temperature relation of a known amount was taken in a glass vessel attached to a glass-spiral pressure gauge, the whole being kept at a temperature uniform to within 3°; and a freezing-point depression measurement was made in an evacuated apparatus with magnetic stirring.

Analysis.—An ampoule of complex was broken under sodium hydroxide solution, the amine liberated distilled into excess of standard acid, and its amount determined by a back-titration, the hydrogen ion being determined potentiometrically (quinhydrone electrode). The residual solution was divided into aliquot portions. Chloride ion was determined in one half by Volhard's method, and aluminium in the other half gravimetrically with 8-hydroxyquinoline. Bromide and iodine ions were determined with silver nitrate and eosin adsorption indicator.



Materials.—Aluminium chloride. Commercial aluminium chloride was mixed with aluminium turnings and resublimed in a stream of dry hydrogen chloride, the iron chlorides thus being reduced to iron (Gratzianskii, *Ukrain. Chem. J.*, 1934, **9**, 432). The white product was then resublimed in dry nitrogen to remove adsorbed hydrogen chloride. Analysis showed it to be 99·6±1% pure, and no iron was detectable by thiocyanate. However, it was still found necessary to resublime this material seven times *in vacuo*, the last 10% being rejected each time, before all the aluminium chloride could be sublimed without leaving an ash-like residue. We attribute the effect to slightly hydrated aluminium chlorides, which sublime with the anhydrous material, afterwards decomposing into alumina and hydrogen chloride.

To overcome this difficulty, aluminium chloride was synthesised directly from the elements. Chlorine from a cylinder was diluted with nitrogen, dried (P_2O_5), and passed over heated aluminium turnings that had previously been carefully dried. The aluminium chloride, as first formed, was tinged yellow by ferric chloride, which was removed as the product passed over further aluminium in the reaction tube. The product was sublimed into a tube fitted with a "breakable joint" and sealed off under dry nitrogen. This tube could subsequently be attached to the vacuum apparatus (tube *A*).

Aluminium bromide and iodide. These were prepared by a modification of the above procedure, as described by Eley and King (*Trans. Faraday Soc.*, 1951, **47**, 1287).

Pyridine. B.D.H. "AnalaR" product was dried over potassium hydroxide and distilled; it had b. p. 115°.

Tri-methyl- and -ethyl-amine. B.D.H. trimethylamine was distilled off potassium hydroxide in a vacuum apparatus, then off freshly sublimed phosphoric oxide into the storage vessel. This process is reported to remove primary and secondary amines (Brown, Bartholmay, and Taylor, *J. Amer. Chem. Soc.*, 1944, **66**, 435); the base had v. p. at 0° = 680 mm., agreeing with Simon and Huter's value (*Z. Elektrochem.*, 1935, **41**, 28). Triethylamine was treated in the same way to give a product of b. p. 89°.

The Complexes.—The formula given is the monomeric formula, which, in actual fact, probably holds for the molecule of complex in the crystalline state (cf. following discussion).

Aluminium Chloride–Pyridine.—This is a colourless crystalline *substance*, m. p. 118°±0·2° (Found: Al, 12·8; Cl, 50·5; C_5H_5N, 36·8. $C_5H_5N,AlCl_3$ requires Al, 12·7; Cl, 50·1; C_5H_5N, 37·2%).

Vapour density. 0·2796 G. of complex was sealed in a reaction vessel of volume 968·2 ml. The vessel was heated and pressure readings were taken up to 300°, at which temperature a slow side-reaction was detectable, rendering further heating undesirable. It seems very likely, by comparison with NH_3,$AlCl_3$, b. p. 422°, that we had not reached the b. p. of the complex. Therefore the significance of the apparent molecular weight value in Table 1 is that the gaseous complex is probably monomeric (*M* 212), but that some liquid was still present.

Molecular weight in benzene. 0·4799 G. of complex, dissolved in 35·21 g. of benzene, gave a

TABLE 1. *Apparent molecular weight of gaseous* C_5H_5N,$AlCl_3$.*

Temp.	230·3°	237·5°	258·5°	263·0°	270·0°	276·5°	288·5°	301·0°
Apparent *M*	801	788	507	453	466	384	317	284

* Calculated on the assumption that all the 0·2796 g. of complex is gaseous.

f. p. depression of 0·183°, corresponding to *M* 380; *i.e.*, degree of association of monomer (*M* 212) into dimer = 0·88.

Molecular weight in nitrobenzene. Three experiments were made in a conventional apparatus, it being found that, unlike the case with benzene as solvent, the rate of water absorption was not sufficient to cause appreciable hydrolysis during the time concerned. Approximately 1% solutions were examined, and the molecular weights obtained were 240, 250, and 220.

Aluminium Chloride–Trimethylamine.—Trimethylamine was condensed on a film of aluminium chloride at −80° and reaction appeared to occur immediately. The complex is a colourless crystalline substance, m. p. 156·4°±0·2° (Found: Al, 14·1; C, 55·6; NMe_3, 30·3. Calc. for NMe_3,$AlCl_3$: Al, 14·0; Cl, 55·3; NMe_3, 30·7%).

Aluminium Chloride–Triethylamine.—The *complex*, when isolated, was slightly discoloured; it had m. p. 121·6—122·1° (Found: Al, 10·6; Cl, 46·9; NEt_3, 44·7. NEt_3,$AlCl_3$ requires Al, 11·5; Cl, 45·4; NEt_3, 43·1%). On prolonged heating above 300° the complex decomposed to give a fluorescent liquid.

Aluminium Bromide–Pyridine.—This *complex*, m. p. 115—117° (Found: Al, 7·5; Br, 70·1; C_5H_5N, 22·9. C_5H_5N,$AlBr_3$ requires Al, 7·8; Br, 69·4; C_5H_5N, 22·7%), and the *trimethylamine* analogue, m. p. 156·9°±0·2° (Found: Al, 8·5; Br, 73·4; NMe, 18·1. NMe_3,$AlBr_3$ requires Al, 8·3; Br, 73·6; NMe_3, 18·1%), were isolated as colourless crystals.

Aluminium Bromide–Triethylamine.—A side reaction occurred with the evolution of some gas, not condensable at a pressure of 25 mm. in a liquid-oxygen bath. The product was a liquid, with some tarry matter.

Aluminium Iodide–Pyridine.—This *complex*, m. p. 110·5—112° (Found: Al, 5·6; I, 78·3; C_5H_5N, 16·6. C_5H_5N,AlI_3 requires Al, 5·55; I, 78·2; C_5H_5N, 16·25%), and the *trimethylamine* analogue, m. p. 156·4°±0·2° (Found: Al, 5·7; I, 81·7; NMe_3, 12·8. NMe_3,AlI_3 requires Al, 5·8; I, 81·5; NMe_3, 12·7%), were also colourless crystals.

Aluminium Iodide–Triethylamine.—Evolution of some permanent gas occurred, and the only product was a tarry residue.

DISCUSSION

Melting Points.—In Table 2 are collected melting-point data for the complexes, together with published data on the NH_3→AlX_3 complexes (Klemm and Tanke, *Z. anorg. Chem.*, 1931, **200**, 343) and the simple halides Al_2X_6 (Fischer and Rahlfs, *ibid.*, 1932, **205**, 37).

TABLE 2. *Melting points of* AlX_3 *complexes.*

Ligand	Halide		
	$AlCl_3$	$AlBr_3$	AlI_3
"AlX_3"	193°	97°	191°
C_5H_5N	118	115—117	110·5—112
NEt_3	121·6—122·1	—	—
NMe_3	156·4	156·9	156·4
NH_3	125	124	126

The peculiar behaviour over the series Al_2Cl_6, Al_2Br_6, Al_2I_6 has been attributed to the presence of an ionic lattice in Al_2Cl_6, whereas the other two halides have a molecular lattice (Fischer and Rahlfs, *loc. cit.*; Fischer, *ibid.*, 1931, **200**, 332). *X*-Ray and other work supports this view (Al_2Cl_6, Ketelaar, MacGillavry, and Renes, *Rec. Trav. chim.*, 1947, **66**, 501; Al_2Br_6, Gerding and Smit, *Z. physikal. Chem.*, 1941, *B*, **50**, 171; Renes and MacGillavry, *Rec. Trav. chim.*, 1945, **64**, 375). All the NH_3→AlX_3 complexes probably

have molecular lattices (Klemm, Clausen, and Jacobi, *Z. anorg. Chem.*, 1931, **200**, 367) and this seems very likely to be so for the complexes we have prepared. We might then have expected a rise in melting point with molecular weight over any given series, X = Cl to I, for example, for C_5H_5N,AlX_3. It is rather striking that the melting point stays nearly constant over this series in all cases. The melting point T_m is given by the ratio of $\Delta H/\Delta S$, where ΔH is the heat-content change and ΔS the entropy change on melting. It may be that the expected increase in ΔH arising from increased van der Waals forces through the series X = Cl to I is somehow offset by a decrease in the ease with which the molecules pack into the lattice, ΔH remaining constant. If ΔS also remained constant, then T would stay constant. Alternatively, ΔH may show the expected increase but be offset by an increase in ΔS, but we cannot take the matter further without a determination of ΔH.

The Monomeric Formula.—The results on $C_5H_5N,AlCl_3$ suggest a considerable association into dimer in the gas phase and in benzene, but in nitrobenzene the substance is probably monomeric. The data on heats of mixing (Dilke, Eley, and Sheppard, *loc. cit.*) make it very unlikely that nitrobenzene will displace pyridine from the dissolved complex. The view that $C_5H_5N,AlCl_3$ is monomeric in nitrobenzene and does not undergo a displacement by the solvent, is supported by the work of Van Dyke and Crawford (*J. Amer. Chem. Soc.*, 1951, **73**, 2022). It seems very likely that the association in benzene and the gas phase is a dipolar association. This would agree with the high dipole moments, *ca.* 7 D, which might be expected from Nespital's results on $C_2H_5{\cdot}NH_2,AlCl_3$ and other complexes (*Z. physikal. Chem.*, 1932, *B*, **16**, 153). Ulich's freezing-point measurements (*ibid.*, Bodenstein Festband, 1931, 423) on aluminium chloride complexes in benzene (amine complexes were not investigated) established a partial association into dimers, which decreased as the solution was diluted, again suggesting dipolar association. Klemm, Clausen, and Jacobi (*loc. cit.*) found a monomeric formula for gaseous $NH_3,AlCl_3$, but in their case, the complex was so stable that its vapour density could be taken at a temperature above 390°. Our results would suggest that $C_5H_5N,AlCl_3$ would be monomeric in the gas at this temperature.

Dissociation of the Complexes.—In contrast to the result in Table 1, C_5H_5N,BF_3 has been investigated up to 356° without side reactions occurring (van der Meulen and Heller, *J. Amer. Chem. Soc.*, 1932, **54**, 4404). At 356° the complex was 56% dissociated into its components, and a bond energy for N→B of 50·6 kcal. was calculated. The bond energy of $C_5H_5N,AlCl_3$, in the light of the results in Table 1, which may be taken to imply no dissociation at 300°, is probably at least this. An estimate of 56·6 kcal. has been made from the heats of mixing of the components (cf. Dilke, Eley, and Sheppard, *loc. cit.*—figure revised in the light of more recent work by Mr. D. J. A. Dear). The successful dissociation of the boron trifluoride compounds depends (*a*) on their low boiling points and (*b*) on the relatively low catalytic activity of the boron trifluoride on the side reactions of the organic base.

Chemical Stability.—The NEt_3,AlX_3 complexes are unstable, entering into some side reaction, increasingly over the series Cl < Br < I. This series may be the order of the strength of the N→Al bond; thus, from heats of mixing by Mr. Dear we estimate for $C_5H_5N{\rightarrow}AlX_3$, 56·6, 71, and 77·1 kcal. for X = Cl, Br, and I, respectively. The order Cl < I < Br is found for the velocity of the Gattermann–Koch reaction, where I lies intermediately, possibly because of decomposition of the iodide (Dilke and Eley, *J.*, 1949, 2613).

Without further work, the nature of the side reaction must remain obscure. Nosaki (*J. Amer. Chem. Soc.*, 1942, **64**, 2920) has investigated the effect of heating the di-*n*-butylamine–aluminium chloride complex. At 190° a marked redistribution of alkyl groups occurs to give complexes of the primary and tertiary bases. This reaction is almost negligible with $NHEt_2,AlCl_3$. Above 200° with the *n*-butylamine complex he noted a slow side reaction to give high-boiling products, which he suggested might be an alkylation of the alkyl group of the tertiary amine. This is possibly what happened with our triethylamine complexes at *ca.* 300°.

In preliminary work on a monobutylamine complex, $C_4H_9{\cdot}NH_2,AlCl_3$, we attributed

the indefinite composition and variable melting point of our products to the presence of alkyl-migration side reactions of the Nozaki type. However, it seems likely that the side reaction is negligible with the ethylamine and methylamine derivatives. Nespital (*loc. cit.*, p. 168) has isolated $C_2H_5 \cdot NH_2, AlCl_3$, m. p. 63°, by distillation at 230°. Goubeau and Siebert (*Z. anorg. Chem.*, 1950, **261**, 63) prepared complexes of mono-, di-, and tri-methylamine with aluminium chloride but did not note any marked side reactions. They stated, however, that the last complex was not quite pure, and in fact its m. p. was 22° below that recorded by us.

We are attempting to apply this method to the preparation of ferric chloride complexes.

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THE UNIVERSITY, BRISTOL, 8. [*Received, January 14th*, 1952.]

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353. *West African Plant Gums. Part I.* Khaya grandifoliola *and* Anogeissus schimperi.

By R. J. MCILROY.

Gums from *Khaya grandifoliola* (mahogany) and *Anogeissus schimperi* have been subjected to graded hydrolysis and the component sugars examined by paper partition chromatography. Hydrolysis of the former gum yields galactose and a degraded polysaccharide constituted of galactose, rhamnose, and galacturonic acid. The latter gum yields, on hydrolysis, arabinose, galactose, and a degraded polysaccharide containing arabinose, galactose, and glucuronic acid.

COMMERICAL gum gatti is obtained from *Anogeissus latifolia*. On hydrolysis with sulphuric acid it yields L-arabinose and an aldobionic acid (equiv., 352). The gum is reported to contain 50% of pentosan and 12% of galacturonic acid (or galactose) (Hanna and Shaw, *Proc. S. Dakota Acad. Sci.*, 1941, **21**, 78).

The water-soluble gum exuded from the bark of *Anogeissus schimperi* was precipitated from aqueous solution by acidified ethanol as a white powder. The aqueous solution was lævorotatory and did not reduce Fehling's solution. Upward mutarotation on hydrolysis indicated β-linkages. Hydrolysis by N-sulphuric acid liberated arabinose and galactose. The degraded polysaccharide which remained was cleaved by 2N-sulphuric acid to arabinose, galactose, and glucuronic acid. The gum from *Anogeissus schimperi* is thus similar to mesquite gum in composition (Anderson and Sands, *Ind. Eng. Chem.*, 1925, **17**, 1257; *J. Amer. Chem. Soc.*, 1926, **48**, 3172; Anderson and Otis, *ibid.*, 1930, **52**, 4461). The component sugars were detected by descending paper partition chromatography.

Khaya gum was prepared as a white powder from the exudate of *Khaya grandifoliola* by dissolution in weak alkali, acidification, and precipitation with ethanol. The aqueous solution was strongly dextrorotatory, with downward mutarotation on hydrolysis indicating α-linkages in the polysaccharide. Hydrolysis of Khaya gum with N-sulphuric acid liberated galactose, which was converted into mucic acid by nitric acid. The degraded polysaccharide was hydrolysed by 2N-sulphuric acid to galactose, rhamnose, and a uronic acid believed to be galacturonic acid. The identity of the uronic acid is based on the characteristic colour reaction with basic lead acetate and has not been confirmed. The component sugars were detected by paper partition chromatography as described above. In composition, the exudate from *K. grandifoliola* resembles slippery elm (*Ulmus fulva*) mucilage (Gill, Hirst, and Jones, *J.*, 1939, 1469; Tipson, Christman, and Levene, *J. Biol. Chem.*, 1939, **128**, 609).

EXPERIMENTAL

Paper Partition Chromatography.—This was carried out on Whatman No. 1 filter-paper strips in phenol–water medium. The solvent front was permitted to advance 30 cm. from the starting-line at 28°. The positions of the sugars were revealed by spraying with aniline hydrogen phthalate in *n*-butanol and development at 105°. Hexoses and pentoses gave rise to brownish and reddish spots respectively, while rhamnose gave a characteristic lemon-yellow

spot. R_F values varied slightly from one chromatogram to the next but the relative positions of the spots were reasonably constant. In every case where a sugar was indicated by the R_F value the identity was established by running further chromatograms with reference-sugar spots.

Khaya Gum.—The gum softens and swells in cold water and dissolves in hot water with difficulty to give a clear, neutral solution. The crude gum was dissolved in cold sodium hydroxide solution (4%), filtered, acidified with acetic acid, and precipitated by ethanol (1½ vols.). Reprecipitation from acidified solution did not reduce the ash content (10·5%). The gum did not reduce Fehling's solution and gave a negative Millon's test for protein; it had $[\alpha]_D^{28}$ +104° (*c*, 0·50 in 4% NaOH). The naphtharesorcin test for uronic acid was positive.

Graded hydrolysis. (*a*) Khaya gum (2·5 g.; ash, 10·8%) was heated with N-sulphuric acid (250 c.c.) for 7 hours in a boiling-water bath; $[\alpha]_D^{30}$ changed from +100° to +81·5°. The neutralised (barium carbonate), filtered hydrolysate was evaporated under reduced pressure and the residue (2·27 g.) extracted with boiling methanol (4 × 50 c.c.). Evaporation of the extracts gave a semi-crystalline mass (A) (1·0 g.), $[\alpha]_D^{28}$ +76° (*c*, 1·24) in water. This (A) was taken up in water (70 c.c.) and subjected to paper-partition chromatotraphy. The sole spot had R_F 0·45, identical with that of galactose on the same paper. The identity of the sugar was confirmed by oxidation of (A) with nitric acid–water (2 : 1) to mucic acid, m. p. 213—214° (from water).

A portion of the methanol-insoluble barium salt was dissolved in water, acidified with sulphuric acid, filtered, and treated with basic lead acetate. The white precipitate which formed dissolved in an excess of reagent. Heating the precipitate gave a brick-red deposit, indicating presence of D-galacturonic acid.

(*b*) The foregoing barium salt (0·81 g.) was treated with 2N-sulphuric acid (50 c.c.), the whole was filtered, and the filtrate heated for 8·5 hours in a boiling-water bath; $[\alpha]_D^{21}$ changed from +61° to +34°. The hydrolysate, neutralised (barium carbonate), filtered, and evaporated under reduced pressure, was extracted with boiling methanol (4 × 50 c.c.). Evaporation of the extracts yielded crystalline sugars (0·156 g.) which were taken up in water (50 c.c.) and analysed on the paper-partition chromatogram as before. Two spots were developed with R_F 0·45 and 0·64 respectively, identical with galactose and rhamnose on the same paper.

Anogeissus *Gum.*—The gum was precipitated from aqueous solution by ethanol (1½ vols.), acidified by acetic acid, as a white flocculum which dried to a white powder (ash, 3·2%). Reprecipitation from acid reduced the ash content to 2·4%. The aqueous solution gave a positive naphtharesorcin test for uronic acid and was strongly lævorotatory $[\alpha]_D^{21}$ *ca.* −64° (*c* = 0·23). The gum did not reduce Fehling's solution and gave a negative Millon's test for protein.

Graded hydrolysis. (*a*) *Anogeissus* gum (5 g.; ash, 2·4%) was heated with N-sulphuric acid (250 c.c.) for 11 hours on a boiling-water bath; $[\alpha]_D^{20}$ became +25° (const.). During hydrolysis a brown flocculent substance (1·4%) separated and was filtered off. This was presumed to be lignin. The hydrolysate was neutralised (barium carbonate) and filtered, and the filtrate evaporated to dryness (5·02 g.) under reduced pressure and extracted with boiling methanol (4 × 150 c.c.). Evaporation of the methanol extracts gave a syrup (2·68 g., 53·6%). Analysis of the insoluble barium salt gave: Ba, 20·3%; OMe, 0; equiv., *ca.* 343.

The syrup (2·68 g.) in water (100 c.c.), analysed by paper-partition chromatography, gave two spots having R_F 0·45 and 0·56 respectively, identical with galactose and arabinose respectively on the same paper.

The basic lead acetate test, applied as for Khaya gum, gave a cream-coloured precipitate which became yellow-brown on heating, indicative of glucuronic acid.

(*b*) The barium salt (2·0 g.) was treated with 2N-sulphuric acid (200 c.c.), the whole filtered, and the filtrate heated for 7 hours in a boiling water bath; $[\alpha]_D^{20}$ (−17·5°) changed to −7·0°. The hydrolysate was neutralised (barium carbonate) and filtered, and the filtrate evaporated to dryness under reduced pressure and extracted with boiling methanol (4 × 50 c.c.). Evaporation of the extracts gave a residue (0·2 g.) which was chromatographed in water (10 c.c.) as before. Two spots were developed, with R_F 0·46 and 0·57 respectively, identical with galactose and arabinose on the same chromatogram.

The gums were collected by the Forestry Department, Ibadan, and by Mr. Oseni of University College, Ibadan, to whom grateful acknowledgment is made.

UNIVERSITY COLLEGE, IBADAN, NIGERIA, WEST AFRICA. [*Received, January 25th,* 1952.]

354. *The Chemistry of Extractives from Hardwoods. Part VII.* Constituents of Muninga, the Heartwood of* Pterocarpus angolensis. *B: 2:4-Dihydroxyphenyl 1-p-Methoxyphenylethyl Ketone (Angolensin).*

By F. E. King, T. J. King, and A. J. Warwick.

Angolensin, a further constituent of the resin extracted from the heartwood of *Pterocarpus angolensis* (*J.*, 1952, 96) and initially obtained in the form of its mono-methyl and -ethyl ethers, has been identified as 2:4-dihydroxyphenyl 1-*p*-methoxyphenylethyl ketone, a structure confirmed when later the parent natural product was isolated.

The heartwood of *Pterocarpus angolensis* contains a high proportion (19%) of alcohol-soluble material from which the previously unknown 6:4′-dihydroxy-5:7-dimethoxy*iso*flavone, muningin, was recently obtained (King, King, and Warwick, Part VI *). Attempts have since been made to isolate other crystalline constituents, for example by sublimation of the crude products obtained from the ethanolic extract through treatment with various solvents, but owing to their involatile nature the distillation of these fractions, even at low pressure, invariably resulted in extensive decomposition. The effect of methylation as a means of increasing the volatility of their phenolic components was investigated by alkylation of the benzene-soluble fraction with methyl iodide and potassium carbonate in acetone, whereupon distillation at 0·3 mm. gave a readily crystallisable product, m. p. 71°, of molecular formula $C_{17}H_{18}O_4$, containing two methoxyl groups. Nevertheless, despite the action of the methylating agent this derivative gave a positive ferric reaction and dissolved, though difficultly, in aqueous sodium hydroxide, properties which indicated the presence of a chelated phenolic hydroxyl group. The existence of this relatively inert substituent was confirmed by the preparation of two derivatives of the ether $C_{17}H_{18}O_4$, *viz.*, a liquid monoacetate and a fully methylated liquid ether, $C_{18}H_{20}O_4$.

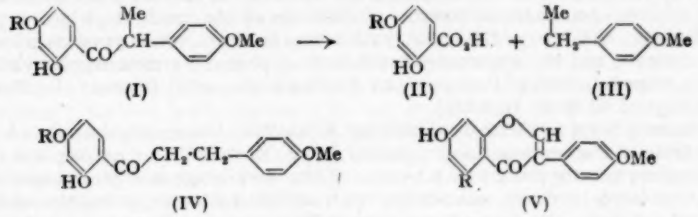
Similarly, treatment of the crude benzene-soluble fraction with ethyl iodide–potassium carbonate afforded after distillation a crystalline ether, $C_{18}H_{20}O_4$, m. p. 97°, which like the methyl compound, m. p. 71°, also exhibited the reactions of a chelated phenolic group. Since the molecular formula of the new product contains but one carbon atom more than the corresponding methyl ether, it follows that only one hydroxyl group is substituted under moderate alkylation conditions and the second methoxyl of the methyl ether, m. p. 71°, is therefore a constituent of the parent substance. To the latter the name angolensin has been given, and the ethers, m. p. 71° and 97°, were respectively termed *O*-methyl- and *O*-ethyl-angolensin.

Analytical experiments were first carried out with methylangolensin which on treatment with hot nitric acid yielded 3-nitro-*p*-anisic acid. Oxidation with potassium permanganate in acetone solution gave *p*-anisic acid and *p*-methoxyacetophenone. Fusion of methylangolensin with sodium hydroxide liberated an oil which distilled from the fusion mixture and had the properties of *p*-ethylanisole (III) (Klages, *Ber.*, 1903, **36**, 3593). It was identified by demethylation with pyridine hydrochloride to the corresponding crystalline phenol which was synthesised, and also by means of the phenylurethane of the products from both natural and synthetic sources.

When the alkali melt was dissolved in water and the solution acidified, 4-methyl-β-resorcylic acid (II; R = Me) was isolated and its identity confirmed by synthesis (Gomberg and Johnson, *J. Amer. Chem. Soc.*, 1917, **39**, 1687). These data resulted in the consideration of two structures for methylangolensin, namely (I; R = Me) and (IV; R = Me), of which, however, the former appeared more convincingly to account for the observed degradation products. Moreover, the formation of a normal acetyl derivative of methylangolensin supports this conclusion since an *o*-hydroxy-ketone of type (IV) would doubtless cyclise to a chromone under acetylation conditions, as happens for example with phloretin (see King and Robertson, *J.*, 1934, 403).

* Part VI, *J.*, 1952, 96.

The orientation of the methyl group in angolensin was ascertained by experiments with the monoethyl ether. When *O*-ethylangolensin was oxidised with potassium permanganate in acetone solution *p*-anisic acid and *p*-methoxyacetophenone were again obtained, the formation of these products at once indicating the location of the methoxylated nucleus. This was further demonstrated by alkali fusion of *O*-ethylangolensin which



(I) (II) (III)

(IV) (V)

gave *p*-ethylanisole and 4-ethyl-β-resorcylic acid (II; R = Et). Accordingly, angolensin is 2 : 4-dihydroxyphenyl 1-*p*-methoxyphenylethyl ketone (I; R = H), a structure which it was later possible to confirm when, by a method depending on its phenolic properties and ready solubility in organic solvents, the parent natural product, m. p. 117°, was isolated from the ethanolic extract, in yields approximating to 3% of the timber. The alternative formula, 2 : 4-dihydroxyphenyl 2-*p*-methoxyphenylethyl ketone (IV; R = H), was thereby finally excluded, a compound of this structure, m. p. 83°, having been described by Shinoda and Sato (*J. Pharm. Soc. Japan*, 1928, **48**, 791). Recently, angolensin was found as a crystalline deposit from the light petroleum solution obtained after very prolonged treatment of the powdered wood with this solvent in a Soxhlet apparatus (D. H. Godson and L. Jurd).

From the recognition of angolensin as (I; R = H) it follows that the liquid dimethyl derivative formed on prolonged methylation is identical with the 2 : 4-dimethoxyphenyl 1-*p*-methoxyphenylethyl ketone prepared by Wessely, Hirschel, Schlögl-Petziwal, and Prillinger (*Monatsh.*, 1938, **71**, 215) during their work on equol. Both angolensin and its methyl ether (I; R = Me) were demethylated by boiling hydriodic acid to 2 : 4-dihydroxyphenyl 1-*p*-hydroxyphenylethyl ketone.

Further fractionation of the alcoholic extract of muninga has resulted in the isolation of prunetin, 5 : 4′-dihydroxy-7-methoxy*iso*flavone (L. Jurd). The occurrence of angolensin in association with *iso*flavones (muningin, prunetin) emphasises the structural relationship of the new compound to this series of natural products, both having the same C_{15} skeleton although at different oxidation–reduction states. It is in fact possible to regard angolensin as a tetrahydro-derivative of formonetin, 7-hydroxy-4′-methoxy*iso*flavone (V; R = H), or even as a reduction product of biochanin-A, 5 : 7-dihydroxy-4′-methoxy*iso*flavone (V; R = OH), from which the oxygen atom of the pyrone ring has been removed by hydrogenolysis. Biochanin-A, which has hitherto only once been reported, occurs in germinated *Chana* grain (Siddiqui, *J. Sci. Ind. Res., India*, 1945, **4**, 68; Bose and Siddiqui *ibid.*, p. 231). It has lately been found (forthcoming publication with K. G. Neill) in the heartwood of the South American tree *Ferreirea spectabilis* where it occurs together with two *iso*flavanones.

Experimental

2-Hydroxy-4-methoxyphenyl 1-p-Methoxyphenylethyl Ketone (*O-Methylangolensin*) (I; R = Me).—After the removal of muningin from the alcoholic extract of muninga (see *J.*, 1952, 96), a portion (5 g.) of the residual dark red resin was triturated with hot benzene (2 × 100 c.c.), and the viscous material thus isolated was heated with methyl sulphate (2 c.c.) and potassium carbonate (2 g.) in acetone (50 c.c.) under reflux for 6 hours. The solution was then filtered and evaporated, and the product distilled. The pale yellow distillate (0·8 g.), b. p. 240—250° (bath temp.)/0·3 mm., largely consisted of O-*methylangolensin* which crystallised from a small volume of methanol in colourless small prisms, m. p. 71° (Found: C, 71·3; H, 6·7; OMe, 22·5; *C*-Me, 4·6. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3; OMe, 21·7; *C*-Me, 5·2%). Treatment of the crude alcoholic extract (600 g.) with benzene (3 × 4500 c.c.) followed by methylation gave a

fraction (95·2 g.), b.p. 212°/0·3 mm., from which methylangolensin (63·5 g.), m. p. 71°, was obtained, equivalent to 2% of the wood. Methylangolensin is readily soluble in organic solvents except light petroleum, and is difficultly soluble in aqueous sodium hydroxide. Its alcoholic solutions give a deep wine-red colour with ferric chloride.

A portion of the methanol solution from which distilled methylangolensin had been crystallised was evaporated, and the oily residue (5 g.) dissolved in acetone was further methylated by methyl sulphate–potassium carbonate. Distillation of the product yielded a pale straw-coloured oil (4·6 g., 88%), b. p. 190—195° (bath temp.)/0·3 mm., which gave no colour reaction with ferric chloride, and was apparently 2:4-dimethoxyphenyl 1-*p*-methoxyphenylethyl ketone [cf. Wessely, Hirschel, Schlögl-Petziwal, and Prillinger (*loc. cit.*)] (Found: C, 71·8; H, 7·1. Calc. for $C_{18}H_{20}O_4$: C, 72·0; H, 6·7%).

2 : 4-*Diacetoxyphenyl* 1-p-*Methoxyphenylethyl Ketone* (OO-*Diacetylangolensin*).—A solution in acetic anhydride of the benzene-soluble portion (0·5 g.) of the ethanol extract was boiled with anhydrous sodium acetate (0·5 g.) for 2 hours. When the mixture had been poured into water, the product, isolated by ether, was washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and distilled. OO-*Diacetylangolensin* (0·52 g., corresponding to an angolensin content of 3·6% of the wood) was thus obtained as a pale straw-yellow uncrystallisable oil, b. p. 220—225° (bath temp.)/0·3 mm., readily soluble in organic solvents except light petroleum (Found: C, 67·3; H, 5·5. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%).

4-*Ethoxy*-2-*hydroxyphenyl* 1-p-*Methoxyphenylethyl Ketone* (O-*Ethylangolensin*) (I; R = Et).—When the benzene extract (20 g.) was refluxed for 8 hours in acetone (200 c.c.) and ethyl iodide (25 c.c.) with potassium carbonate (20 g.), and the acetone-soluble product was isolated, washed with water, and distilled, a pale yellow oil (17·1 g.), b. p. 205—218°/0·3 mm., was obtained. When dissolved in methanol it gave O-*ethylangolensin* (9 g.) as colourless hexagonal prisms, m. p. 97° (Found: C, 71·7; H, 6·7. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%). The compound is difficultly soluble in aqueous sodium hydroxide and gives a deep wine-red colour with ferric chloride.

The oil isolated by evaporation of the methanolic solution from which the distilled ethylangolensin had been crystallised was further treated with ethyl iodide–potassium carbonate until the ferric reaction was negative. Isolation in the usual way gave 2 : 4-*diethoxyphenyl* 1-p-*methoxyphenylethyl ketone*, an uncrystallisable oil (7·5 g.), b. p. 200—205° (bath temp.)/0·3 mm. (Found: C, 72·6; H, 7·2. $C_{20}H_{24}O_4$ requires C, 73·1; H, 7·3%).

2-*Acetoxy*-4-*methoxyphenyl* 1-p-*Methoxyphenylethyl Ketone*.—Methylangolensin (0·5 g.), m. p. 71°, was refluxed in acetic anhydride (2 c.c.) with anhydrous sodium acetate (0·5 g.) for 2 hours. The mixture was poured into water, and extraction with ether isolated the *acetyl* derivative as a colourless highly viscous oil (0·47 g., 82%), b. p. 190—195° (bath temp.)/0·3 mm. (Found: C, 69·3; H, 6·5. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%).

Oxidation of Methylangolensin.—(*a*) *With nitric acid*. Methylangolensin (1 g.) was heated with concentrated nitric acid (5 c.c.) for 1 hour on a steam-bath, and the resulting solution diluted with water. The product extracted from the aqueous solution with ether (3 × 50 c.c.) was completely soluble in aqueous sodium hydrogen carbonate; when recovered by ether extraction of the acidified carbonate solution it solidified, and crystallisation from water gave 3-nitro-*p*-anisic acid (0·45 g., 65%), m. p. and mixed m. p. 186°.

(*b*) *With potassium permanganate*. To a solution of methylangolensin (2 g.) in dry acetone (100 c.c.) heated under reflux, powdered potassium permanganate was added until the rate of oxidation became very slow. After the solvent had been evaporated, the residue was treated with water and the manganese dioxide dissolved by the passage of sulphur dioxide. The solution was then extracted with ether (3 × 50 c.c.), and the solution shaken with aqueous sodium hydrogen carbonate. Acidification of the carbonate solution and ether extraction isolated *p*-anisic acid, crystallising from water in needles, m. p. and mixed m. p. 179—181°.

The carbonate-washed ether solution was dried and evaporated, thus leaving a pale brown oil from which *p*-methoxyacetophenone (0·65 g., 62%), m. p. 33—34°, distilled at 100—105° (bath temp.)/0·3 mm. (Found: C, 71·5; H, 6·8. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%). The product gave a semicarbazone, m. p. 195° alone or mixed with an authentic specimen, and the 2 : 4-dinitrophenylhydrazone prepared in ethanolic sulphuric acid crystallised from benzene in bright red rectangular plates, m. p. 230—232° (Found: N, 16·8. Calc. for $C_{15}H_{14}O_5N_4$: N, 17·0%). Borsche and Barthenheier (*Annalen*, 1942, **553**, 254) give m. p. 233—234°.

Alkali Fusion of Methylangolensin.—From treatment for several hours with boiling 40% aqueous sodium hydroxide methylangolensin was recovered as the sodium salt. The compound

(1 g.) was therefore heated with sodium hydroxide (5 g.) and water (1 c.c.) in a copper tube for 1 hour, and the product dissolved in water which was then acidified and extracted with ether. From the ethereal solution washing with aqueous sodium hydrogen carbonate removed a crystalline acid which separated from water in needles (0·42 g., 71%) giving a purple ferric reaction and having m. p. 155—156° alone or mixed with 2-hydroxy-4-methoxybenzoic acid (Gomberg and Johnson, *loc. cit.*). From it, by methylation with methyl sulphate–aqueous sodium hydroxide, 2 : 4-dimethoxybenzoic acid, m. p. 108°, was obtained.

Distillation of the carbonate-washed and dried ethereal extract gave *p*-ethylanisole (0·4 g., 84%), an oil of characteristic odour, b. p. 100—105° (bath temp.)/13 mm. It was more conveniently isolated by heating methylangolensin (5 g.) with a mixture of sodium hydroxide (5 g.), potassium hydroxide (5 g.), and water (1 c.c.), and allowing the volatile product to distil. By redistillation, *p*-ethylanisole ($\eta = 1{\cdot}5100$) was obtained in 92% yield (Found : C, 78·8; H. 8·8. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·8%). Klages (*loc. cit.*) records $\eta = 1{\cdot}5094$, 1·5102.

p-*Ethylphenol.*—*p*-Ethylanisole (2·3 g.) derived from methylangolensin was heated with pyridine hydrochloride (8 g.) on an oil-bath at 220° for 6 hours (cf. Prey, *Ber.*, 1941, **74**, 1219). The mixture was treated with water, and the solution extracted with ether (2 × 50 c.c.) which was then washed with hydrochloric acid. From the ethereal solution 4N-sodium hydroxide (50 c.c.) extracted the product which when liberated by acid was extracted, dried, and distilled. The distillate crystallised from light petroleum in needles, m. p. 47° alone or mixed with a synthetic specimen of *p*-ethylphenol (Found : C, 78·8; H, 8·5. Calc. for $C_8H_{10}O$: C, 78·6; H. 8·2%). Warmed in light petroleum with phenyl *iso*cyanate, the phenol gave *p*-ethylphenyl phenylcarbamate, m. p. and mixed m. p. 120°.

Oxidation of Ethylangolensin.—A solution of ethylangolensin (0·6 g.) in acetone (50 c.c.) was refluxed with powdered potassium permanganate (6 g.) for 1 hour. By the process used in the oxidation of the corresponding methyl ether, a pale yellow oil (0·23 g., 76%) was isolated and identified as *p*-methoxyacetophenone by means of the semicarbazone, m. p. 195°, and 2 : 4-dinitrophenylhydrazone, m. p. 230—232°. The carbonate-soluble oxidation product crystallised from water in needles (0·02 g., 6%), m. p. 182° alone or mixed with *p*-anisic acid.

Alkali Fusion of Ethylangolensin.—A mixture of ethylangolensin (1 g.), sodium hydroxide (5 g.), and water (1 c.c.) was heated in a copper tube under reflux for 15 minutes. *p*-Ethylanisole (0·13 g.) was then isolated by the procedure used in the corresponding experiment with methylangolensin, the distillation residue consisting of unreacted ethylangolensin (0·6 g.). The carbonate-soluble product crystallised from water (charcoal) in colourless needles (0·16 g.), m. p. 154°. Mixed with 2-hydroxy-4-methoxybenzoic acid of m. p. 156—157°, it had m. p. *ca.* 130°, but with 4-ethoxy-2-hydroxybenzoic acid, no m. p. depression was observed.

2 : 4-*Dihydroxyphenyl* 1-p-*Methoxyphenylethyl Ketone* (*Angolensin*) (I; R = H).—The very dark red brittle resin (75 g.) left after the removal of muningin from the alcoholic extract of 400 g. of powdered muninga (see *J.*, 1952, 98) was dissolved in acetone (100 c.c.), and the solution diluted with ether (300 c.c.). The precipitated solid (18 g.) was discarded and the remaining liquid shaken with N-sodium hydroxide (100 c.c.). The product liberated by hydrochloric acid from the aqueous layer was then shaken with ether (2 × 100 c.c.), the ethereal solution being decanted from a tarry residue. Evaporation of the dried ethereal solution left a semi-solid red product and this was triturated with hot benzene (2 × 250 c.c.). Evaporation of the decanted benzene solution gave a brown oil (22 g.) which partly crystallised. A portion (2 g.) of benzene-soluble product was refluxed with light petroleum (b. p. 80—100°), and the pale yellow solution concentrated and set aside overnight. The very pale brown crystalline solid which separated, together with a second crop obtained by further evaporation (total 1·6 g.), when further crystallised from light petroleum gave 2 : 4-*dihydroxyphenyl* 1-p-*methoxyphenylethyl ketone* (*angolensin*) as colourless flat prisms, m. p. 117° (Found : C, 70·5; H, 5·8; OMe, 9·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9; OMe, 11·4%). Angolensin is freely soluble in organic solvents except light petroleum, and dissolves readily in aqueous sodium hydroxide. It gives a deep wine-red colour with ferric chloride, green with nitric acid and a yellow solution in concentrated sulphuric acid.

Methylation with excess of ethereal diazomethane at 0° for 30 minutes and crystallisation of the product from methanol gave methylangolensin (I; R = Me), m. p. and mixed m. p. 71°. Oxidation with nitric acid at 100° gave 3-nitro-*p*-anisic acid which was isolated after the addition of water by ether extraction; the acid had m. p. and mixed m. p. 186°. Alkali fusion under the conditions used for methylangolensin gave a neutral fraction consisting of *p*-ethylanisole. The alkali-soluble product was isolated by repeated ether extraction, and consisted of a pale brown oil which when distilled (bath temp., 180—185°/13 mm.) crystallised from light petroleum in prisms, m. p. 109° undepressed on admixture of a specimen with resorcinol.

2 : 4-*Dihydroxyphenyl* 1-p-*Hydroxyphenylethyl Ketone.*—Methylangolensin (1 g.), m. p. 71°, was heated with hydriodic acid (15 c.c.; *d* 1·7) and acetic acid (5 c.c.) under reflux for 3 hours. The mixture was poured into water and the product, isolated by ether as a deep red oil, was dissolved in methanol, and the solution passed down a short column of activated alumina to remove coloured impurities.

The solvent was then evaporated and the residue triturated with water, whereupon the 2 : 4-*dihydroxyphenyl* 1-p-*methoxyphenylethyl ketone* solidified and was recrystallised from water, forming prisms (0·22 g., 25%), m. p. 139—140° (Found: C, 69·9; H, 5·7. $C_{15}H_{14}O_4$ requires C, 69·75; H, 5·4%). Repetition of the experiment with angolensin also resulted in the formation of the trihydroxy-ketone. It gave a deep wine-red colour with ferric chloride in aqueous alcoholic solution.

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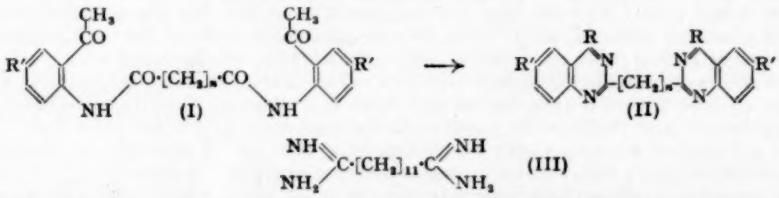
355. *The Preparation of some αω-Di-2-quinazolinylalkanes.*

By K. SCHOFIELD, T. SWAIN, and R. S. THEOBALD.

A number of the compounds named in the title have been synthesised by Bischler's cyclisation (*Ber.*, 1891, **24**, 506) of *NN'*-di-*o*-acetylphenyl-adipo- and -sebaco-diamides. The use of high pressure in this reaction has been avoided by effecting cyclisation in molten ammonium acetate. The same conditions applied to 2-formamidoacetophenone give 4-methylquinazoline.

FOR a number of reasons we were interested in compounds of type (II). Thus, substances of this class bear an obvious relation to numerous therapeutically effective diamidines, *e.g.* (III) (King, Lourie, and Yorke, *Ann. Trop. Med.*, 1938, **32**, 177), and it has recently been stressed that quinazoline should be regarded as a cyclic amidine (Elderfield, Williamson, Gensler, and Kremer, *J. Org. Chem.*, 1947, **12**, 405; Morley and Simpson, *J.*, 1948, 360). Further, we are aiming at the synthesis of αω-diquinazolinylpolyenes, and methods suitable for the synthesis of (II) promised to have limited application in this series also.



Only one compound of type (II) has hitherto been described, König (*J. pr. Chem.*, 1904, **69**, 23) having obtained (II; R = OH; R' = H; *n* = 2) from anthranilic acid and succinonitrile at 150°. The availability of various substituted *o*-aminoacetophenones rendered Bischler's method (*loc. cit.*), involving the cyclisation of an *o*-acylamino-ketone with ammonia under pressure, immediately feasible [I ⟶ II (R = Me)].

The readily available adipic and sebacic acids have so far served as the source of the polymethylene chain, and the related dianilides (I; R' = H, Cl, NO_2, or CN; *n* = 4 or 8) have been prepared from adipoyl or sebacoyl chloride and the relevant *o*-aminoacetophenone. The ease of anilide formation depended decidedly on the nature of the substituent, R', *para* to the amino-group. *o*-Aminoacetophenone reacted violently with both adipoyl and sebacoyl chloride in ethereal solution. 2-Amino-5-chloroacetophenone condensed noticeably less vigorously under these conditions, but the change nevertheless went to completion. A nitro-group however made the amine so weakly basic that, even in boiling pyridine, adipoyl chloride and 2-amino-5-nitroacetophenone reacted only to the extent

of 30%, although the corresponding sebacoyl derivative gave a good yield in boiling toluene. 2-Amino-5-cyanoacetophenone reacted readily with both the acid chlorides in ether, but, in contrast to the other derivatives, the cyano-anilides (I; R′ = CN; $n = 4$ or 8) were appreciably soluble in this medium.

The cyclisation of the anilides, when heated, with aqueous alcoholic ammonia under pressure, was almost quantitative in all cases except that of the adipoyl nitroanilide (I; R′ = NO_2; $n = 4$). This behaviour was at first attributed to the deactivating influence of the nitro-group, but since the corresponding sebacanilide (I; R′ = NO_2; $n = 8$) cyclised quantitatively it is now believed to be due merely to the unusually small solubility of the compound in the reaction medium. Despite sharp melting points, analysis (see Experimental) suggests that the two cyano-quinazolines were not entirely pure.

Clearly, in the absence of large-scale pressure equipment, Bischler's quinazoline synthesis is limited severely in its scale of application. To remove this handicap we have sought new conditions for the reaction, and have effected the cyclisations of this type by passing ammonia through a solution or suspension of the anilides in molten ammonium acetate. In all the cases so far examined, including the adipoyl-nitroanilide which previously presented difficulty, this method resulted in quantitative production of the quinazoline. Quinazolines of the present type are therefore available in any desired quantity.

Our interest in 4-methylquinazoline (Schofield and Swain, *J.*, 1949, 1367, and unpublished work) prompted the application of the new conditions to *o*-formamidoacetophenone. 4-Methylquinazoline was originally obtained by Bogert and Nabenhauer (*J. Amer. Chem. Soc.*, 1924, **46**, 1932) from 4-methylquinazoline-2-carboxyamide, and by Schofield and Swain (*loc. cit.*) by cyclisation of *o*-formamidoacetophenone with ammonia under pressure. Application of our new conditions to the latter intermediate has now provided 4-methylquinazoline in high yield.

Experimental

M. p.s are uncorrected. Cyclisations in molten ammonium acetate were all carried out (except for the cyano-compounds) as described below for 1 : 4-di-(4-methyl-6-nitro-2-quinazolinyl)-butane, and in all cases gave substantially quantitative yields.

NN′-*Di*-o-*acetylphenyladipodiamide*.—Adipoyl chloride, from adipic acid (1·35 g.) (*Org. Synth.*, 1943, Coll. Vol. 2, 169), was dissolved in dry ether (10 c.c.), and added slowly to a solution of *o*-aminoacetophenone (5 g.) in ether (10 c.c.); a vigorous reaction occurred and a white solid separated. The mixture was set aside for 12 hours, and the product (3·17 g.) was then collected, washed with water, and dried. Recrystallisation from alcohol afforded silky white needles, m. p. 151—152°, of the *diamide* (Found: C, 69·3; H, 7·1. $C_{22}H_{24}O_4N_2$ requires C, 69·5; H, 6·3%).

1 : 4-*Di*-(4-*methyl*-2-*quinazolinyl*)*butane*.—The powdered anilide (0·5 g.), aqueous ammonia (1 c.c.; *d* 0·88), and alcohol (10 c.c.) were heated in a sealed tube at 140° for 6 hours. The resulting solution was evaporated to dryness and the residue (0·4 g.; m. p. 109—111°) was crystallised from dilute ethanol, giving the *diquinazolinylbutane*, m. p. 116—117° (Found: C, 76·9; H, 6·2; N, 16·5. $C_{22}H_{22}N_4$ requires C, 77·2; H, 6·3; N, 16·4%).

NN′-*Di*-o-*acetylphenylsebacodiamide*.—Sebacoyl chloride [prepared from the acid (1·87 g.) in a similar manner to adipoyl chloride] in dry ether (25 c.c.) was added to *o*-aminoacetophenone (5 g.) in the same solvent (25 c.c.). The *anilide* (1·7 g.; m. p. 76—78°), isolated as above, crystallised from alcohol in colourless needles, m. p. 89—90° (Found: C, 71·3; H, 7·4. $C_{26}H_{32}O_4N_2$ requires C, 71·6; H, 7·3%).

1 : 8-*Di*-(4-*methyl*-2-*quinazolinyl*)*octane*.—The above anilide (1·5 g.), alcohol (10 c.c.), and aqueous ammonia (2 c.c.) were treated as described for the butane, and provided on concentration to half-volume a yellow solid (1·15 g.; m. p. 99—100°). The pure *product*, obtained by crystallisation from dilute alcohol, formed pale yellow needles, m. p. 101—102° (Found: C, 77·7; H, 7·1. $C_{26}H_{30}N_4$ requires C, 78·3; H, 7·5%).

NN′-*Di*-(2-*acetyl*-4-*chlorophenyl*)*adipodiamide*.—Adipoyl chloride (from 0·22 g. of the acid) in dry ether (10 c.c.) was added to 2-amino-5-chloroacetophenone (1 g.) in ether (10 c.c.). After being shaken for a few minutes the solution became turbid, and a flocculent precipitate separated. Crystallisation of this from chloroform gave a white solid (0·62 g.; m. p. 219—221°), and further crystallisation gave the pure *anilide* as small white crystals, m. p. 220—221° (Found: C, 58·3; H, 4·8. $C_{22}H_{22}O_4N_2Cl_2$ requires C, 58·8; H, 4·9%).

1 : 4-*Di*-(6-*chloro*-4-*methyl*-2-*quinazolinyl*)*butane*.—From the anilide (0·5 g.), alcohol (9 c.c.), and concentrated ammonia (1 c.c.) there was obtained in the usual way a yellowish solid (0·41 g.). The *quinazoline* separated from alcohol as fine white needles, m. p. 166—167° (Found : C, 64·0; H, 4·9. $C_{22}H_{20}N_4Cl_2$ requires C, 64·2; H, 4·9%).

NN′-*Di*-(2-*acetyl*-4-*chlorophenyl*)*sebacodiamide*.—Prepared as in previous examples, from sebacic acid (1·49 g.) and 2-amino-5-chloroacetophenone (5 g.), the crude compound (1·65 g.) was crystallised several times from alcohol, giving a white crystalline *anilide*, m. p. 137—138° (Found : C, 62·0; H, 6·4. $C_{26}H_{30}O_4N_2Cl_2$ requires C, 61·8; H, 5·9%).

1 : 8-*Di*-(6-*chloro*-4-*methyl*-2-*quinazolinyl*)*octane*.—The chloro-anilide (1·5 g.) gave, by the usual procedure, a product (1·17 g.), m. p. 146—147°, after one crystallisation. The *quinazoline* separated from alcohol as pale yellow needles, m. p. 147—148° (Found : C, 66·1; H, 6·1; N, 12·9. $C_{26}H_{28}N_4Cl_2$ requires C, 66·8; H, 6·0; N, 12·0%).

NN′-*Di*-(2-*acetyl*-4-*nitrophenyl*)*adipodiamide*.—Adipoyl chloride (from 0·4 g. of acid), 2-amino-5-nitroacetophenone (1 g.), and pyridine (10 c.c.) were refluxed for 1 hour, and the product (0·3 g.), collected after cooling, was recrystallised from pyridine, giving the pure *anilide*, m. p. 287—288° (Found : C, 56·2; H, 4·7. $C_{22}H_{22}O_8N_4$ requires C, 56·2; H, 4·7%).

1 : 4-*Di*-(4-*methyl*-6-*nitro*-2-*quinazolinyl*)*butane*.—A suspension of the nitroanilide (0·5 g.) in molten ammonium acetate (5 g.) was heated for 4 hours at 160° with dry ammonia, the mixture was then diluted with water, and the product (0·45 g.; m. p. 218—219°) collected. The *quinazoline* crystallised from alcohol as a white crystalline solid, m. p. 219—220° (Found : C, 60·0; H, 4·7. $C_{22}H_{20}O_4N_6$ requires C, 61·1; H, 4·6%). The bomb-tube method gave 0·4 g. of this product together with 1·1 g. of unchanged material from 1·5 g. of the anilide.

NN′-*Di*-(2-*acetyl*-4-*nitrophenyl*)*sebacodiamide*.—Sebacoyl chloride (from 1·4 g. of acid), 2-amino-5-nitroacetophenone (5 g.), and dry toluene (40 c.c.) were refluxed for 1 hour, and the grey solid was collected and triturated with concentrated hydrochloric acid, giving a product (2·5 g.), m. p. 178—182°. The *anilide* formed lustreless filaments, m. p. 183—184° (Found : C, 58·1; H, 5·6. $C_{26}H_{30}O_8N_4$ requires C, 59·3; H, 5·7%), from chloroform.

NN′-*Di*-(2-*acetyl*-4-*cyanophenyl*)*adipodiamide*.—Adipoyl chloride (from 0·34 g. of acid) in dry ether (10 c.c.) was added to 2-amino-5-cyanoacetophenone (1·5 g.) also in ether (100 c.c.). After 12 hours the precipitate of amine hydrochloride was removed and the solution was concentrated, giving the crude product (1·15 g.). Trituration with concentrated hydrochloric acid, followed by washing with water and crystallisation from chloroform, afforded a pale yellow *diamide*, m. p. 246—247° (Found : C, 66·3; H, 5·4. $C_{24}H_{22}O_4N_4$ requires C, 66·9; H, 5·1%).

1 : 4-*Di*-(6-*cyano*-4-*methyl*-2-*quinazolinyl*)*butane*.—The anilide (0·5 g.), treated as usual in a sealed tube, gave the *quinazoline* (0·25 g. after one crystallisation), which separated from alcohol as a buff solid, m. p. 238—239° (Found : C, 72·4; H, 5·4. $C_{24}H_{20}N_6$ requires C, 73·4; H, 5·1%).

NN′-*Di*-(2-*acetyl*-4-*cyanophenyl*)*sebacodiamide*.—Sebacoyl chloride (from 0·48 g. of acid) in dry ether (10 c.c.) was added to 2-amino-5-cyanoacetophenone (1·5 g.) in the same solvent (100 c.c.). The *anilide* (1·55 g.), isolated as before, separated from alcohol as a yellow solid, m. p. 179—180° (Found : C, 68·5; H, 6·3. $C_{28}H_{30}O_4N_4$ requires C, 69·1; H, 6·2%).

1 : 8-*Di*-(6-*cyano*-4-*methyl*-2-*quinazolinyl*)*octane*.—The anilide (0·5 g.), cyclised under pressure, gave the *quinazoline* (0·23 g. after one crystallisation from dilute ethanol), which was a cream-coloured solid, m. p. 197—198° (Found : C, 73·4; H, 6·6. $C_{28}H_{28}N_6$ required C, 74·9; H, 6·3%).

4-*Methylquinazoline*.—A suspension of *o*-formamidoacetophenone (8·9 g.) in molten ammonium acetate (90 g.) was maintained at 155—160° for 3 hours, during the passage of a vigorous stream of ammonia. The resulting yellow solution was diluted with water and extracted with ether, and the ethereal solution was washed with dilute sodium hydroxide solution and dried (Na_2CO_3). Removal of the ether and distillation of the residue (7·2 g.) gave a clear pale yellow oil (6·9 g.), b. p. 140—142°/20 mm. The product was characterised as 4-methylquinazoline by conversion into the picrate (Schofield and Swain, *loc. cit.*).

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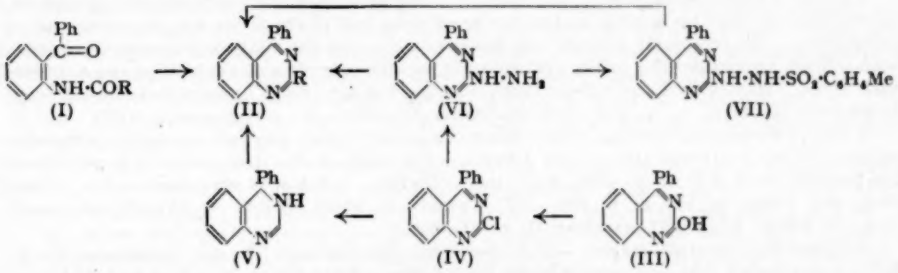
356. 4-*Phenylquinazoline*.

By K. Schofield.

Four methods of preparing 4-phenylquinazoline are described. The most practicable one consists in the catalytic reduction of 2-chloro-4-phenylquinazoline to 3 : 4-dihydro-4-phenylquinazoline, followed by oxidation of the latter with alkaline potassium ferricyanide.

The behaviour of phenyl-substituted heterocyclic compounds on nitration is of some theoretical interest (Schofield, *Quart. Reviews*, 1950, **4**, 382). 4-Phenylquinazoline has therefore been synthesised so that its nitration (to be reported later) can be studied.

By the cyclisation of *o*-acetamidobenzophenone (I; R = Me) with ammonia under pressure, Bischler and Barad (*Ber.*, 1892, **25**, 3080) obtained 2-methyl-4-phenylquinazoline (II; R = Me). Subsequent oxidation, and decarboxylation of the resulting acid, made possible the isolation of 4-phenylquinazolinium picrate, but the free base was not described. Clearly, it would be advantageous if the use of pressure equipment could be obviated, and encouraging experience with *o*-acylaminoacetophenones (Schofield, Swain, and Theobald, preceding paper) suggested that *o*-formamidobenzophenone (I; R = H) might be converted directly into 4-phenylquinazoline (II; R = H) by passage of ammonia through its solution in molten ammonium acetate. The result was disappointing, for although 4-phenylquinazoline was formed (< 20%) in this reaction, it was contaminated with *o*-aminobenzophenone, and purification was difficult. The difficulty of cyclisation as compared with derivatives of *o*-aminoacetophenone must be attributed to the lower carbonyl-group reactivity of the benzophenone, but the method might still be useful with acyl derivatives other than the formamido-compound.



Attention was next centred on 2-hydroxy-4-phenylquinazoline (III), originally prepared by Gabriel and Stelzner (*Ber.*, 1896, **29**, 1300) by heating *o*-aminobenzophenone and urea. Improvements in the preparation of this compound and of the derived 2-chloro-4-phenylquinazoline (IV) are described below. By reducing the chloro-compound with red phosphorus and hydriodic acid, Gabriel and Stelzner (*loc. cit.*) obtained 3 : 4-dihydro-4-phenylquinazoline (V). We have found this method to be less satisfactory on the large than on the small scale, and prefer the catalytic procedure detailed in the Experimental section (*cf.* Elderfield, Williamson, Gensler, and Kremer, *J. Org. Chem.*, 1947, **12**, 405). Gabriel (*Ber.*, 1903, **36**, 800) oxidised 3 : 4-dihydroquinazoline to quinazoline by means of potassium ferricyanide in alkaline solution, and Elderfield *et al.* (*loc. cit.*) applied the method to *Bz*-substituted 3 : 4-dihydroquinazolines. The same reagent oxidised (V) to 4-phenylquinazoline in high yield. The sequence of reactions [III ⟶ IV ⟶ V ⟶ II (R = H)] is the preferred method of preparing 4-phenylquinazoline.

The catalytic reduction of 2-chloro-4-phenylquinazoline to 3 : 4-dihydro-4-phenylquinazoline under the conditions so far examined, whilst satisfactory, did not give such high yields as were obtained by Elderfield and his co-workers (*loc. cit.*) in certain cases, and two alternative routes were considered.

The 2-chloro-compound (IV) was readily converted in high yield into 4-phenyl-2-

quinazolylhydrazine (VI), and oxidation of this compound with copper sulphate (*cf.* Schofield and Swain, *J.*, 1950, 392) gave 4-phenylquinazoline, but in poor yield. 2-Chloro-4-phenylquinazoline did not react satisfactorily with toluene-*p*-sulphonhydrazide, but (VII) was easily prepared from (VI). Decomposition of (VII) in alkaline solution (*cf.* Dewar, *J.*, 1944, 619; Albert, Brown, and Duewell, *ibid.*, 1948, 1284; Clinton, *J. Amer. Chem. Soc.*, 1949, **71**, 755; Albert and Royer, *J.*, 1949, 1148) produced 4-phenylquinazoline, but the four-stage process [IV ⟶ VI ⟶ VII ⟶ II (R = H)] was not as efficient as that through 3 : 4-dihydro-4-phenylquinazoline.

4-Phenylquinazoline was characterised as its picrate (Bischler and Barad, *loc. cit.*), and 2-chloro-4-phenylquinazoline by conversion into 2-ethoxy-4-phenylquinazoline. The salts of 4-phenylquinazoline give characteristic yellow solutions with acids.

A single attempt to condense formamide with *o*-aminobenzophenone failed, not unexpectedly in view of Gabriel's experience (*loc. cit.*) with *o*-aminobenzaldehyde.

Experimental

M.p.s are uncorrected.

o-*Formamidobenzophenone.*—*o*-Aminobenzophenone (10 g.) and formic acid (80 c.c.; 95—100%) were refluxed for 1 hour and the excess of acid was then removed at reduced pressure. The residual oil (11·2 g.) slowly crystallised. o-*Formamidobenzophenone* formed white prisms, m. p. 54—55° (Found : C, 74·6; H, 5·1. $C_{14}H_{11}O_2N$ requires C, 74·6; H, 4·9%), when crystallised from ether–light petroleum (b. p. 40—60°).

2-*Hydroxy*-4-*phenylquinazoline.*—*o*-Aminobenzophenone (50 g.) and urea (25 g.) were heated at 190—200° with vigorous stirring in a vessel large enough to accommodate the considerable initial frothing. A crust slowly formed on the reaction mixture, and by the end of the experiment (*ca.* 1 hour) the whole had solidified. The product was thoroughly digested with alcohol (150 c.c.) and collected [50·8 g.; m. p. 250—252° (Gabriel and Stelzner, *loc. cit.*, give m. p. 250—251°)].

2-*Chloro*-4-*phenylquinazoline.*—The hydroxy-compound (20 g.) was refluxed with phosphorus oxychloride (80 c.c.) for ½ hour, and rather more than half of the latter was then removed by distillation. The remaining solution was poured on ice, and the mixture was carefully basified with sodium hydroxide (the yellow acid solution became colourless at neutrality) and extracted with ether. Removal of the solvent from the dry extract (Na_2SO_4) gave 2-chloro-4-phenylquinazoline (*ca.* 20 g.), m. p. 114—115° (Gabriel and Stelzner, *loc. cit.*, give m. p. 113°).

2-*Ethoxy*-4-*phenylquinazoline.*—The chloro-compound (0·5 g.) was refluxed with a solution of sodium (0·2 g.) in ethanol (10 c.c.) for 2 hours. The mixture was then poured into water, and the product (0·48 g.; m. p. 105—107°) was collected. 2-*Ethoxy*-4-*phenylquinazoline* formed crisp, pale yellow tablets, m. p. 106—107° (Found : C, 77·0; H, 6·0. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6%), from light petroleum (b. p. 40—60°).

4-*Phenyl*-2-*quinazolylhydrazine.*—2-Chloro-4-phenylquinazoline (3 g.), hydrazine (3 g.; 90%), and ethanol (100 c.c.) were refluxed for 7 hours. After the mixture had cooled the precipitate was collected and washed with a little water, giving 2·8 g. of product, m. p. 154—156°. 4-*Phenyl*-2-*quinazolylhydrazine* formed yellow needles (evidently slightly impure), m. p. 155—156° (Found : C, 72·2; H, 5·2. $C_{14}H_{12}N_4$ requires C, 71·1; H, 5·1%), when crystallised from alcohol.

The hydrazine (2·5 g.), dissolved in warm pyridine (75 c.c.), was treated with toluene-*p*-sulphonyl chloride (2·25 g.), and the solution was set aside at room temperature for 12 hours and then heated at 95° for ½ hour. The product, obtained by dilution with water, gave a fawn solid (2·5 g.), m. p. 202—203° (decomp.), when digested with hot alcohol. The *toluene*-p-*sulphonyl* derivative formed glistening fawn crystals, m. p. 203—205° (decomp.) (Found : C, 64·6; H, 4·9. $C_{21}H_{18}O_2N_4S$ requires C, 64·6; H, 4·6%), on crystallisation from alcohol.

3 : 4-*Dihydro*-4-*phenylquinazoline.*—(i) 2-Chloro-4-phenylquinazoline (1 g.), red phosphorus (1 g.), and hydriodic acid (8 c.c.; *d* 1·7) were refluxed for 2½ hours. When cool, the mixture was basified with ammonia and extracted with ether. Removal of the solvent from the dried extract (Na_2CO_3) gave an oil which soon crystallised to a white solid (0·27 g., 62%), m. p. 165—167°, after one crystallisation from ethyl acetate (Gabriel and Stelzner, *loc. cit.*, give m. p. 165—166°). The stated yield was regularly obtained in small-scale experiments, but could not be reproduced on the large scale (*e.g.* a similar experiment with 20 g. of the chloro-compound gave only 6·7 g. of product).

(ii) The chloro-compound (8 g.) was dissolved in warm methanol (400 c.c.) and the solution

was shaken with palladium–calcium carbonate (24 g.; Busch and Stöve, *Ber.*, 1916, **49**, 1063) and hydrogen. Reduction was complete in 1·5—1·75 hours. (During the reaction the solution became yellow, but towards the end it became grey—colour changes presumably attending the formation and reduction of 4-phenylquinazoline.) After removal of the catalyst and evaporation of the methanol the oily residue was shaken with sodium hydroxide solution and ethyl acetate. On concentration, the dried (Na_2SO_4) ethyl acetate extract deposited 3 : 4-dihydro-4-phenylquinazoline (4·8 g.), m. p. 161—164°.

4-Phenylquinazoline.—(i) Preliminary experiments showed that acetamide and *o*-aminobenzophenone were contaminants of the 4-phenylquinazoline obtained by cyclisation of *o*-formamidobenzophenone. The latter (5·1 g.) and previously fused ammonium acetate (50 g.) were maintained at 175—180° for 8 hours during the passage of a vigorous stream of ammonia. During this time the initial suspension became clear. The product was cooled, diluted with water, and extracted with ether. The ethereal solution was washed with sodium hydroxide solution, then with water, and finally itself extracted with hydrochloric acid. The yellow acid solution was basified with sodium hydroxide and re-extracted with ether. The dried (Na_2SO_4) ethereal solution was concentrated to a small volume and treated whilst hot with light petroleum (b. p. 40—60°) until a permanent turbidity resulted. When the solution cooled, a yellow solid formed (3·2 g.; m. p. 70—80°) which gave a positive diazotisation test. This material (0·5 g.) was dissolved in hydrochloric acid (4 c.c. of concentrated acid and 6 c.c. of water), and the mixture was washed with ether and then diazotised at 0° with aqueous sodium nitrite (0·35 g. in 3 c.c. of water). After being heated for 1 hour at 95° and then washed with ether, the solution was basified and extracted with the latter solvent. Removal of the ether after drying (Na_2CO_3) gave a white solid (0·23 g.; m. p. 92—93°). Recrystallisation (charcoal) from light petroleum (b. p. 40—60°) gave a white crystalline product, m. p. 97—99°, identical with that described in (ii).

(ii) 3 : 4-Dihydro-4-phenylquinazoline (5 g.) was dissolved by warming it in a mixture of water and dioxan (100 c.c. of each). Potassium hydroxide solution (11 g. in 32·5 c.c. of water) was added and the mixture was heated on the steam-bath during the quick addition of a solution of potassium ferricyanide (16·5 g.) in water (132 c.c.). Heating, with occasional shaking, was continued for 5 minutes, and the turbid mixture was then diluted with water, basified with sodium hydroxide solution, and extracted with ether. Removal of the solvents, finally at reduced pressure, from the dried (Na_2SO_4) extract gave a fairly pure product (4·8 g.), m. p. 97—99°. *4-Phenylquinazoline* formed pearly, glistening leaflets, m. p. 99—100° (Found: C, 77·0; H, 6·0. $C_{14}H_{10}N_2$ requires C, 76·8; H, 5·6%), when crystallised from light petroleum (b. p. 40—60°) containing a trace of ether.

The picrate was formed in alcohol solution. From this solvent it gave soft felted yellow needles, m. p. 176—178° (with some preliminary sublimation) (Found: C, 55·2; H, 3·3. Calc. for $C_{14}H_{10}N_2,C_6H_3O_7N_3$: C, 55·2; H, 3·0%). Bischler and Barad (*loc. cit.*) give m. p. 178°.

(iii) 4-Phenyl-2-quinazolylhydrazine (0·2 g.) was heated at 95° with water (2 c.c.), and the mixture treated during 5 minutes with copper sulphate (0·27 g. in 2·7 c.c. of water). After being heated for 15 minutes more the mixture was basified with sodium hydroxide solution and extracted with ether. Removal of the solvent after drying (Na_2SO_4) gave 4-phenylquinazoline (35 mg.), m. p. 97—98°, identical with a specimen from (ii).

(iv) The toluene-*p*-sulphonyl derivative (0·4 g.) described above was added to a warm solution containing dioxan (10 c.c.), water (40 c.c.), and anhydrous sodium carbonate (4 g.). On boiling, the solution became deep red, effervescence occurred, and finally the whole became brown. Boiling was continued for 20 minutes and the mixture was then diluted with water and extracted with ether. Removal of the solvent from the dry (Na_2SO_4) extract, finally under reduced pressure, gave a sticky solid (0·16 g.), which on recrystallisation (charcoal) from ether–light petroleum (b. p. 40—60°) provided 4-phenylquinazoline (0·14 g.), m. p. 95—97° alone and when mixed with an authentic specimen.

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357. *Cyclic Polymerisation of Acetylene. Examination of the* $C_{10}H_{10}$ *Fraction.*

By D. S. Withey.

The presence of 1-phenylbuta-1 : 3-diene and vinyl*cyclo*octatetraene in the $C_{10}H_{10}$ fraction formed during the preparation of *cyclo*octatetraene from acetylene (Craig and Larrabee, *J. Amer. Chem. Soc.*, 1951, **73**, 1191; Cope and Fenton, *ibid.*, p. 1195) has been confirmed. Reactions of vinyl*cyclo*octatetraene with bromine, with hydrogen, and with maleic anhydride are described and discussed. Some halogen derivatives of 1-phenylbuta-1 : 3-diene are described.

Reppe, Schlichting, and Meister (*Annalen*, 1948, **560**, 93) isolated two hydrocarbons $C_{10}H_{10}$ from by-products obtained during the polymerisation of acetylene to *cyclo*octatetraene, and considered these to be isomeric *cyclo*decapentaenes. Craig and Larrabee (*J. Amer. Chem. Soc.*, 1951, **73**, 1191) and Cope and Fenton (*ibid.*, p. 1195) have shown that the $C_{10}H_{10}$ fraction is a mixture of *cis*-1-phenylbuta-1 : 3-diene and vinyl*cyclo*octatetraene. Our work concerned with the preparation and identification of the $C_{10}H_{10}$ fraction was almost complete when the above results became available. Some new results are now reported.

Treatment of the fraction with two mols. of bromine gave the two known stereoisomers of 1 : 2 : 3 : 4-tetrabromo-1-phenylbutane and a third unidentified bromide $C_{10}H_{10}Br_4$. As widely differing melting points are quoted for the tetrabromides of phenylbutadiene, these were prepared from *trans*-1-phenylbuta-1 : 3-diene and purified by fractional crystallisation.

trans-1-Phenylbuta-1 : 3-diene was also treated in turn with hydrogen chloride and bromine, to form what is thought to be 1 : 2-dibromo-3-chloro-1-phenylbutane.

In the presence of four mols. of bromine, vinyl*cyclo*octatetraene rapidly formed a tetrabromide which then added one further mol. of bromine at a slower rate. At this stage, reaction had apparently ceased and the product was shown to be a hexabromide. When 12 mols. of bromine were used, a break in the rate of addition was still evident at the tetrabromide stage but in this case a total of four mols. of bromine was added. The product was an octabromide, which resisted further addition. The bromides of *cyclo*octatetraene are derivatives of *bicyclo*[4 : 2 : 0]octane, and by analogy the new bromides may be derivatives of an ethyl*bicyclo*[4 : 2 : 0]octane; the resistance of the octabromide supports this theory.

Reppe, Schlichting, and Meister (*loc. cit.*) treated their $C_{10}H_{10}$ hydrocarbons with maleic anhydride and in both cases obtained the adduct $C_{10}H_{10}{,}3C_4H_2O_3$ as the main crystalline product whilst the adduct $C_{10}H_{10}{,}2C_4H_2O_3$ crystallised from the mother-liquors (in the case of the orange-yellow isomer) in smaller amounts. We find that under similar conditions vinyl*cyclo*octatetraene gives the adduct $C_{10}H_{10}{,}2C_4H_2O_3$. None of the other adduct has yet been isolated from the reaction product although its formation seems reasonable.

Hydrogenation of vinyl*cyclo*octatetraene in methanol or acetic acid over a palladium catalyst indicated the presence of five double bonds. In both solvents the rate of hydrogenation decreased considerably after saturation of the fourth double bond, at which stage the product was presumably 1-ethyl*cyclo*octene which has been identified in the products of incomplete hydrogenation of the $C_{10}H_{10}$ fraction by Craig and Larrabee (*loc. cit.*).

Experimental

M. p.s are uncorrected.

The $C_{10}H_{10}$ fraction was isolated by fractionation of the products obtained by polymerisation of acetylene in the presence of tetrahydrofuran, nickel cyanide, and calcium carbide. It formed an orange-yellow, mobile liquid with a wide boiling range (47·5°/3·8 mm. to 48·5°/2 mm.) and n_D^{20} 1·5780.

Bromination of the $C_{10}H_{10}$ *Fraction.*—Bromine (32 g.) in chloroform (35 c.c.) was added during 1¼ hours to a stirred solution of the $C_{10}H_{10}$ fraction (13 g.) in chloroform (35 c.c.)

at −50° to −55°. After the mixture had been kept at room temperature overnight, no free bromine remained, and by washing with water and removal of the solvent under reduced pressure the product was obtained as a dark green syrup (45·8 g.). Treatment of this with cold ether gave two crops of colourless crystals.

The first crop (3·5 g.; m. p. 122—133°), after five crystallisations from ethanol, yielded 1 : 2 : 3 : 4-tetrabromo-1-phenylbutane as colourless rhombs, m. p. 151—152° (Found : C, 26·7; H, 2·2; Br, 71·2. Calc. for $C_{10}H_{10}Br_4$: C, 26·7; H, 2·2; Br, 71·1%). The mixed m. p. with an authentic sample (see below) was 151—152°.

From the mother-liquors, a small quantity of an unidentified *tetrabromide*, $C_{10}H_{10}Br_4$, m. p. 91° (unchanged by crystallisations from ligroin, ethanol, or acetic acid), was obtained as fine colourless needles (Found : C, 26·6; H, 2·2. $C_{10}H_{10}Br_4$ requires C, 26·7; H, 2·2%).

The second crop (7·8 g.; m. p. 58—63°) was recrystallised from ethanol and then from light petroleum (b. p. 60—80°), to give colourless needles, m. p. 74—75°, which did not depress the m. p. of an authentic sample of the lower-melting stereoisomer of 1 : 2 : 3 : 4-tetrabromo-1-phenylbutane (Found : C, 26·7; H, 2·4; Br, 71·4%).

Preparation of trans-1-*Phenylbuta*-1 : 3-*diene and Some of its Halides.*—The hydrocarbon was prepared in 41% yield by Klages's method (*Ber.*, 1904, **37**, 2309), which gives the *trans*-form (Grummitt and Christoph, *J. Amer. Chem. Soc.*, 1951, **73**, 3479). It formed a colourless liquid, b. p. 41—42°/0·8 mm., n_D^{16} 1·6098.

The tetrabromides were prepared by treating it (4 g.) with bromine (9·9 g.) in carbon tetrachloride at 0—10°. Formation of the dibromide took place rapidly, but absorption of the second molar equivalent of bromine required several hours. After a week, a crop of colourless crystals had separated (*A*; 2·5 g.; m. p. 139—140°). The mother-liquor deposited a further quantity of colourless crystals (*B*; 11·2 g.; m. p. 64—68°). Fractional crystallisation of *A* gave colourless rhombs, m. p. 151·5—152° (from ethanol–benzene), and of *B* gave colourless needles, m. p. 75° (from ligroin). M. p.s recorded for these stereoisomers are : 142° (Liebermann and Rüiber, *Ber.*, 1900, **33**, 2400), 146° (Klages, *Ber.*, 1902, **35**, 2651), 76° and 151° (Rüiber, *Ber.*, 1903, **36**, 1406), 146° (Heide, *Ber.*, 1904, **37**, 2101), 146—147·5° and 147·2—147·7° (Grummitt and Christoph, *loc. cit.*).

An ethereal solution of *trans*-3-chloro-1-phenylbut-1-ene was prepared from *trans*-1-phenylbuta-1 : 3-diene (10 g.) in ether (30 c.c.) by passing in dry hydrogen chloride at −10° until no more was absorbed (cf. Muskat and Huggins, *J. Amer. Chem. Soc.*, 1934, **56**, 1240). The resulting straw-coloured solution was washed with water, dried (Na_2SO_4), and treated with a solution of bromine (12·3 g.) in carbon tetrachloride. Next day colourless needles (4·7 g.), m. p. 136—140°, were separated. By recrystallisation in turn from ethanol, light petroleum, and benzene–light petroleum, (?) 1 : 2-*dibromo*-3-*chloro*-1-*phenylbutane* was obtained as colourless needles, m. p. 150—151° (Found : C, 36·4; H, 3·3%; 10·655 mg. gave 16·926 mg. of silver halide. $C_{10}H_{11}Br_2Cl$ requires C, 36·8; H, 3·4%; 16·93 mg. of silver halide).

*Vinyl*cyclo*octatetraene.*—The $C_{10}H_{10}$ fraction (79 g.) was dissolved in an equal volume of light petroleum (b. p. 40—60°), and the solution cooled to about −80° for 12 hours. A bright yellow crystalline solid separated and, after separation by decantation, was again crystallised as above. The recrystallised material was distilled under reduced pressure. After a forerun (0·5 g.; n_D^{20} 1·5716) the main fraction, b. p. 31·5°/0·7 mm., m. p. −20° to −19°, n_D^{20} 1·5724, was collected. One more low-temperature crystallisation from light petroleum gave vinyl-*cyclo*octatetraene (32 g.; 40% of starting material), b. p. 27°/0·5 mm., m. p. −19° to −18°, n_D^{20} 1·5723, d_4^{20} 0·9325 (Found : C, 92·2; H, 7·8. Calc. for $C_{10}H_{10}$: C, 92·3; H, 7·7%).

It was unchanged on storage in nitrogen in the dark for several months, but in light and air rapidly afforded a pale yellow solid.

*Bromination of Vinyl*cyclo*octatetraene.*—(*a*) A solution of vinyl*cyclo*octatetraene (1·622 g.) in carbon tetrachloride (total volume 25 c.c.) was added rapidly with agitation to a solution of bromine in carbon tetrachloride (175 c.c.) which contained sufficient bromine to saturate four double bonds of the sample. The mixture was kept agitated at room temperature in artificial light and 5-c.c. aliquots were periodically treated with excess of potassium iodide solution, and the liberated iodine was determined by titration against 0·1N-sodium thiosulphate. It was thus found that, under the conditions employed, two double bonds were saturated almost instantly, whereas the third required 25 minutes. Very little further bromination was detected after 12 hours. After removal of excess of bromine and evaporation of the solvent, the *hexabromide* was obtained as a colourless gum which crystallised when treated with methanol. Recrystallisation from ethanol gave laths, m .p. 122—123° (Found : C, 19·9; H, 1·7; Br, 78·7. $C_{10}H_{10}Br_6$ requires C, 19·7; H, 1·6; Br, 78·7%.)

(*b*) Bromine (96 g.) in carbon tetrachloride (90 c.c. of solution) was delivered into a solution of vinyl*cyclo*octatetraene (6·5 g.) in carbon tetrachloride (50 c.c.) at −10° to 0°. Two molar equivalents of bromine were decolorised rapidly, after which the reaction slowed down and the remaining bromine was added all at once. The reaction mixture was diluted to 250 c.c. and kept at room temperature in the dark. After 20 and 40 hours, the unused bromine was determined by treatment of 2-c.c. aliquots with potassium iodide and titration against standard sodium thiosulphate. Utilization of bromine was found to be 31·5 and 30·8 g. respectively (Calc. for $C_{10}H_{10}Br_8$: 32 g.). After removal of excess of bromine by sodium hydroxide solution and water, the solution was dried and evaporated in a vacuum, leaving a colourless gum (34·9 g., 90·7%) which crystallised when treated with ether. Successive crystallisations of this from benzene and finally from acetic acid gave an *octabromide* as colourless rhombs, m. p. 176—177° (decomp.) (Found: C, 15·8; H, 1·4; Br, 83·6. $C_{10}H_{10}Br_8$ requires C, 15·6; H, 1·3; Br, 83·1%).

*Maleic Anhydride Adduct of Vinyl*cyclo*octatetraene.*—Maleic anhydride (6 g.) and vinyl*cyclo*octatetraene (2·6 g.) were heated together in an oil-bath at 140°; a vigorous reaction set in which caused the mixture to boil for some 30 seconds. Heating was then continued for an hour, the bath-temperature being slowly raised to 160°. After cooling, the colourless crystals which had first formed after 50 minutes' heating, were collected and washed with dry acetone [yield 1·5 g.; m. p. 281—288° (decomp.)]. After several recrystallisations from acetic acid, the pure adduct was obtained as small colourless parallelograms, m. p. 303—305° (decomp.) (after rapid heating to 260°) (Found: C, 66·4; H, 4·4%; equiv., 81·4. Calc. for $C_{10}H_{10},2C_4H_2O_3$: C, 66·3; H, 4·3%; equiv., 81·5).

*Hydrogenation of Vinyl*cyclo*octatetraene.*—When vinyl*cyclo*octatetraene (2·00 g.), 5% palladium–barium sulphate (0·7 g.), and methanol or acetic acid (20 c.c.) were shaken in an atmosphere of hydrogen, absorption of hydrogen corresponding to four double bonds occurred during 2 hours and a slower absorption corresponding to the fifth double bond during the following 4 hours, after which reaction ceased.

I am indebted to Mr. H. Wright-Hodgson for the microanalyses, Dr. W. O. Jones for helpful advice, and the Directors of the British Oxygen Company Ltd. for the supply of raw material and laboratory facilities.

British Oxygen Company, Ltd.,
Lombard Road, London, S.W.19.

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358. *The Direct Calculation of True Dipole Moments from Measurements on Solutions or Pure Liquids.**

By A. D. Buckingham and R. J. W. Le Fèvre.

An empirical relationship is presented whereby for a given molecule μ_{gas} may be obtained from $\mu_{solution}$ or μ_{liquid}. Comparisons made by application to a number of polar liquids, representative of different molecular shapes, show that the new equation is superior to others previously proposed.

A number of empirical equations, connecting apparent dipole moments obtained from solutions in benzene with the true values determined in the gaseous states, were recently reviewed by Angyal, Barclay, and Le Fèvre (*J.*, 1950, 3370). The most satisfactory seemed to be that—listed as (1) below—proposed earlier by Barclay and Le Fèvre (*J.*, 1950, 556). Unfortunately, however, its applicability did not extend beyond non-polar solvents. Attempts have accordingly been made to remedy this defect. As a result, a new expression can now be submitted, which, used wholly or in part, enables the ratios μ_{liquid}/μ_{gas} or $\mu_{solution}/\mu_{gas}$ to be calculated *a priori* more accurately than by other relationships previously recorded. In support of this claim, tests on the representative series of molecules used before (references above) will now be summarised.

* In this and subsequent papers on dipole moments from these laboratories, subscripts 1 and 2 will refer, respectively, to the solvent and solute. This is the reverse of the convention formerly adopted in our papers.—R. J. W. Le F.

Equations Examined.—In these, subscripts 1 and 2 indicate solvent and solute respectively, ε is the dielectric constant, d the density, and n the refractive index, e is the base of Napierian logarithms, and x^2 a quantity dependent on the shape of the dissolved molecule under consideration. Values of x^2 have been derived from scale-drawings incorporating Stuart's "Wirkungsradien" (*Z. physikal. Chem.*, 1935, *B*, **27**, 350); if A is the measurement along the axis of $\mu_{resultant}$ and C is the lesser of the other two dimensions perpendicular to A, then generally $x^2 = (C^2 - A^2)/(\text{greatest length})^2$. The ξ used by Ross and Sack (*Proc. Phys. Soc.*, 1950, **63**, 893) also reflects the molecular structure; it can be ascertained quickly from curves reproduced in the paper just cited.

The equations now to be considered are numbered for subsequent reference:

$$(1)\quad \frac{\mu^2_{soln.}}{\mu^2_{gas}} = 1 + \frac{\varepsilon_1 - 1}{\varepsilon_1 + 2}\left(e^{x^2} - \frac{n_1^2}{n_2^2}\right)$$

$$(2)\quad \frac{\mu^2_{soln.}}{\mu^2_{gas}} = 1 + \frac{\varepsilon_1 - 1}{\varepsilon_1 + 2}\left[e^{x^2} - (e - e^{x^2})^{3(n_1^2 - n_2^2)(1 - e^{x^2})^2}\right]$$

$$(3)\quad \frac{\mu^2_{soln.}}{\mu^2_{gas}} = 1 + \frac{\varepsilon_1 - 1}{\varepsilon_1 + 2}\left[e^{x^2} - (e - e^{x^2})^{3(n_1^2 - n_2^2)(1 - e^{x^2})^2}\right] - \frac{1{\cdot}69\, e^{x^2}(\varepsilon_1 - 1)(n_2^2 + 1)|\varepsilon_1 - n_2^2|}{\varepsilon_1^2 n_2^2 (e^{x^2} + 1)(e^{M_2/d_2 A_2 B_2 C_2})}$$

$$(4)\quad \frac{\mu_{soln.}}{\mu_{gas}} = \frac{3\varepsilon_1}{(\varepsilon_1 + 2)} \cdot \frac{1 + (n_2^2 - 1)\xi}{\varepsilon_1 + (n_2^2 - \varepsilon_1)\xi}$$

$$(5)\quad \frac{\mu^2_{liq.}}{\mu^2_{gas}} = 1 + \frac{\varepsilon - 1}{\varepsilon + 2}(e^{x^2} - 1) - \frac{1{\cdot}69\, e^{x^2}(\varepsilon - 1)(n^2 + 1)(\varepsilon - n^2)}{\varepsilon^2 n^2 (e^{x^2} + 1)(\varepsilon^{M/dABC})}$$

$$(6)\quad \frac{\mu^2_{liq.}}{\mu^2_{gas}} = \text{as No. (5) but with numerical constant} = 1{\cdot}70$$

$$(7)\quad \mu^2_{gas} = \frac{9kTM}{4\pi Nd} \cdot \frac{(\varepsilon - n^2)(2\varepsilon + n^2)}{\varepsilon(n^2 + 2)^2}$$

Equation (1) was advanced by Barclay and Le Fèvre (*J.*, 1950, 556). Although this gave results in good agreement with experiment for many solutes, yet there were some (*e.g.*, paraldehyde, sulphur dioxide, and trimethylamine) where it was less satisfactory. We therefore sought a substitute for the term n_1^2/n_2^2 in (1). In this—and other empirical approaches underlying the present paper—we have been guided by intuitive guesses very similar to those set out before (*J.*, 1950, 3370). These we would now amend to read: (*a*) that x^2, being concerned with areas, may be a measure of hindrance to rotation, so that $\exp x^2$ (or perhaps $1 - \exp x^2$) may reflect the non-randomness of rotational modes about the greatest and least axis of length of the solute molecule, and (*b*) that a second term is needed having some relation to the exclusion from spherical distribution of the centres of the molecules surrounding the solute in the directions collinear and perpendicular to its resultant moment, and—in consequence—to the disturbance from isotropy of its polarisable solvent environment.

For the requirement of (*b*) the introduction of $(e - e^{x^2})$ seemed reasonable, since such a factor could express the degree of elongation of the molecule in a direction at right angles to the dipole axis. Because x^2 must (by its definitition) be less than unity, it followed that e would be the maximum value for $\exp x^2$. Thus for an imaginary plane structure (*i.e.*, one with negligible thickness), whose resultant dipole axis is perpendicular to the plane, $(e - e^{x^2})$ would be zero; its values for other extreme shapes were obvious: notably it could never become negative so that quantities such as:

$$(e - e^{x^2})^{9(\varepsilon_1 - n_2^2)(1 - e^{x^2})^2/\varepsilon_1} \quad \text{(A)}$$

or

$$(e - e^{x^2})^{3(n_1^2 - n_2^2)(1 - e^{x^2})^2} \quad \text{(B)}$$

would be entirely real.

(A) and (B) were the two most promising alternatives to n_1^2/n_2^2 found after many trials. When equations containing them were applied to the test substances in Table IV of the paper by Barclay and Le Fèvre (*loc. cit.*) both proved better than the original equation (1).

However, if used on solutions of nitrobenzene in several solvents (Cleverdon and Smith, *Trans. Faraday Soc.*, 1949, **45**, 109), an equation with (B) was superior to one with (A). Thus we selected equation (2) as the best replacement for (1).

Nevertheless, equation (2) was still limited in usefulness to cases where the solvent was non-polar. To make it general an extra term was accordingly devised. This addition clearly had to vanish if ε were unity (when $\mu_{soln.} = \mu_{gas}$), and to be zero or very small if the solvent were non-polar. These desiderata were met by utilising the factors $(\varepsilon - 1)$ and $(\varepsilon - n^2)$. Of many possible " third terms " tried, that shown in equation (3) was the most successful.

The full form of the new equation now proposed is (3); in application to pure liquids this becomes (5) or (6). For solutions in non-polar solvents the third term is small and equation (2) may be used successfully. In equations (1), (2), (3), and (5) refractive indexes for the Na_D line are employed. The change in the numerical constant from equation (5) to equation (6) is caused by taking, whenever available, $n^2_{eff.}$ instead of n^2_D in the latter [the " effective " refractive index is estimated by equating the distortion polarisation to $(n^2_{eff.} - 1)M/(n^2_{eff.} + 2)d_{liq.}$]. Equation (4) is due to Ross and Sack (*loc. cit.*); here also $n^2_{eff.}$ has been introduced as far as possible, but when it is unknown the procedure recommended by Ross and Sack has been followed and the n^2 corresponding to $1{\cdot}05[R_L]_D$ has been adopted. Equation (7) is Onsager's (*J. Amer. Chem. Soc.*, 1936, **58**, 1486); it is included now for comparison because Böttcher (*Physica*, 1939, **6**, 59) has already shown it to be fairly satisfactory for many polar substances. Here again $n^2_{eff.}$, rather than n^2_D, has been used if available.

Table 1 sets out the numerical data required for testing the equations. The apparent dipole moments shown under $\mu_{liq.}$ or $\mu_{C_6H_6}$ have been calculated from the differences between the total polarisations of the substances (as pure liquids or at infinite dilution in benzene) and the distortion polarisations recorded from measurements on gaseous dielectrics, except in those instances where gaps occur under $n^2_{eff.}$ in Table 1 when $[R_L]_D$ has of necessity replaced ${}_DP$ (for source references, see Barclay and Le Fèvre, *loc. cit.*; Angyal, Barclay, and Le Fèvre, *loc. cit.*). The values of ξ quoted to three figures are those estimated from the geometrical dimensions of the molecules by Ross and Sack (*loc. cit.*); the remainder have been derived from the corresponding lengths A, B, and C by the method described by these authors.

Table 2 shows the relative success with which the various equations will give μ_{gas} from $\mu_{C_6H_6}$ or $\mu_{liq.}$.

TABLE 1. *Numerical data required.*

Substance	M_2	d_4^{25}	$(n^2_D)^{25}$	$(n^2_{eff.})^{25}$	ε^{25}	$\mu_{liq.}$	$\mu_{C_6H_6}$	A	B	C	ξ
CH_3Cl	50·49	0·8785	1·751	1·929	9·68 [1]	1·19	1·69	5·27	3·80	3·80	0·267
CH_2Cl_2	84·94	1·3175	2·0295	2·349	8·93 [1]	$1{\cdot}14_5$	1·55	4·10	6·10	3·60	0·38
$CHCl_3$	119·39	1·4790	2·0825	2·368	$4{\cdot}724$ [1]	$0{\cdot}97_5$	1·13	4·10	6·50	6·50	0·364
$CH_3{\cdot}CN$	41·05	0·7772	1·800	—	36·7 [2]	1·36	3·11—3·51	5·95	3·80	3·80	0·22
$CH_3{\cdot}NO_2$ ...	61·04	1·1362	1·9040	—	27·75 [3]	$1{\cdot}32_5$	3·02—3·13	5·20	4·50	3·80	0·27
$COMe_2$	58·08	0·7863	1·8400	—	19·11 [4]	1·52	2·74	5·15	6·54	3·80	0·315
Paraldehyde	132·16	0·9896	1·989	2·499	12·93 [5]	$1{\cdot}74_5$	1·87	3·80	9·50	9·50	0·59
SO_2	64·06	1·369	1·763	1·911	13·20 [6]	1·14	1·61	3·44	5·00	3·08	0·354
NMe_3	59·11	0·6267	1·808	—	2·44 [7]	0·72	0·86	3·82	6·55	6·55	0·47
$Ph{\cdot}CH_3$	92·13	0·8657	2·2320	—	2·366 [8]	0·34	0·34	8·25	6·05	3·80	0·20
PhCl	112·56	1·1011	2·3180	2·554	5·612 [3]	1·15	1·59	8·08	6·05	3·16	0·181
$Ph{\cdot}NO_2$	123·11	1·1986	2·4045	2·633	34·89 [9]	1·69	3·95	8·00	6·05	2·90	0·236
$Ph{\cdot}CN$	103·12	1·0013	2·329	—	25·20 [8]	1·71	3·74—3·97	8·95	6·05	2·90	0·15

References: n^2_D and $n^2_{eff.}$ values: Barclay and Le Fèvre (*J.*, 1950, 556).

ε values: [1] Barclay and Le Fèvre (*loc. cit.*). [2] Le Fèvre and Le Fèvre (*J.*, 1935, 1747). [3] Ulich and Nespital (*Z. physikal. Chem.*, 1932, *B*, **16**, 221). [4] Åkerlof (*J. Amer. Chem. Soc.*, 1932, **54**, 4125). [5] Le Fèvre, Mulley, and Smythe (*J.*, 1950, 290). [6] Le Fèvre and Ross (*J.*, 1950, 283). [7] Le Fèvre and Russell (*Trans. Faraday Soc.*, 1947, **43**, 374). [8] Le Fèvre (*ibid.*, 1938, **34**, 1127). [9] Drude (*Z. physikal. Chem.*, 1897, **23**, 309).

TABLE 2. *Calculations of* μ_{gas} *by equations* (1)—(7).

Substance	By (1)	By (2)	By (3)	By (4)	By (5)	By (6)	By (7)	μ_g (found)
CH_3Cl	1·89	1·85	1·92	1·85	1·96	1·91	1·76	1·86
CH_2Cl_2	1·59	1·57	1·60	1·48	1·58	1·55	1·57	1·57
$CHCl_3$	1·02	1·01	1·03	1·09	0·98	0·94	1·08	1·01
$CH_3{\cdot}CN$	3·49—3·94	3·49—3·94	3·60—4·06	3·58—4·04	3·96	3·98	3·58	3·94—3·98
$CH_3{\cdot}NO_2$ ...	3·30—3·42	3·27—3·39	3·36—3·49	3·29—3·41	3·17	3·19	3·04	3·42
$COMe_2$	2·95	2·87	2·98	2·88	3·04	3·04	2·98	2·85—3·02
Paraldehyde	1·60	1·48	1·52	1·50	1·65	1·59	2·72	1·44
SO_2	1·70	1·63	1·69	1·64	1·59	1·58	1·90	1·62
NMe_3	0·78	$0{\cdot}74_5$	0·77	0·80	0·67	0·67	0·74	0·64
$C_6H_5{\cdot}CH_3$ ...	0·37	0·37	0·37	$0{\cdot}38_5$	0·37	0·37	0·34	0·37
C_6H_5Cl	1·74	1·72	1·73	1·81	1·67	1·64	1·34	1·73
$C_6H_5{\cdot}NO_2$ ...	4·29	4·25	4·27	4·21	4·24	4·24	3·96	4·24
$C_6H_5{\cdot}CN$ ...	4·09—4·34	4·07—4·32	4·07—4·32	4·43—4·70	4·31	4·33	3·58	4·39

Finally, Table 3 presents the ratios of ${}_0P_{soln.}/{}_0P_{gas}$ (*i.e.*, $\mu^2_{soln.}/\mu^2_{gas}$) forecast by equations (1), (2), (3), and (4) for one solute, nitrobenzene, in a range of polar and non-polar solvents, the properties of which have been conveniently listed by Cleverdon and Smith (*loc. cit.*).

TABLE 3. *Calculations of* ${}_0P_{soln.}/{}_0P_{gas}$ *for solutions of nitrobenzene by equations* (1)—(4).

Solvent	$E_{25}{}^{solvent}$	$(n^2_D)_{25}{}^{solvent}$	By (1)	By (2)	By (3)	By (4)	${}_0P_s/{}_0P_g$ (found)
n-Hexane	1·887	1·8847	0·92	0·95	0·90	0·95	0·91
Di*iso*amyl	1·976	1·9973	0·90	0·93	0·89	0·94	0·88
*cyclo*Hexane	2·016	2·0221	0·89	0·92	0·89	0·93	0·88
Decalin	2·162	2·16	0·87	0·89	0·87	0·90	0·86
Dioxan	2·204	2·0171	0·88	0·91	0·90	0·89	0·85
CCl_4	2·228	2·1656	0·86	0·88	0·87	0·89	0·86
p-Xylene	2·260	2·2317	0·85	0·87	0·86	0·88	0·85
C_6H_6	2·273	2·2417	0·85	0·87	0·85	0·88	0·87
CS_2	2·633	2·6360	0·76	0·72	0·70	0·81	0·75
Et_2O	4·250	1·8295	0·82	0·90	0·78	0·53	0·57
$CHCl_3$	4·724	2·0825	0·75	0·81	0·68	0·48	0·55
C_6H_5Cl	5·612	2·3180	0·67	0·69	0·47	0·39	0·34
$C_6H_5{\cdot}NO_2$	34·89	2·4045	0·47	0·47	0·16	0·020	0·16

Conclusions.—From Table 2 it may be seen that values of μ_{gas} predicted by equations (2) and (3) agree in the main with the observed values within differences not in excess of the experimental errors. The latter are of the order of 2%, 1% in the value of $\mu_{C_6H_5}$, and 1% in the observed value of μ_{gas}. Moreover, both (2) and (3) give figures for μ_{gas} which are, on the whole, more correct than those computed by either (1) (the Barclay–Le Fèvre equation) or (4) (the Ross–Sack equation).

Equation (5)—and also (6), which by utilising $n^2_{eff.}$ instead of n^2_D gives slightly better results than (5)—forecasts values for μ_g (from observations solely on the pure liquids) which are essentially of a similar accuracy to those predicted by the equation of Barclay and Le Fèvre on benzene solutions. Equation (5) certainly yields results which are superior to those derived by (7) (the Onsager equation).

From the evidence of Tables 2 and 3, it appears (*a*) that by use of data obtained from solutions in benzene, the most probable value for μ_g is obtained by application of equation (2), and (*b*) by use of data obtained from pure liquids, the most satisfactory equation to apply is (5). Equation (6), utilising $n^2_{eff.}$, will not be a form useful in practice because a knowledge of $n^2_{eff.}$ implies the existence of "gas" measurements, which would themselves permit a direct calculation of μ_g.

We conclude by referring to the case of water, since among the 33 substances for which Böttcher (*loc. cit.*) estimated μ_{gas} *via* the Onsager formula, this gave the worst result, *viz.*, $(\mu_{gas})_{calc.} = 3{\cdot}0$—$3{\cdot}1$D, in contrast to the observed figure of 1·8 D. In our recalculations the following data are used: $\varepsilon^{25} = 78{\cdot}42$ (Åkerlof and Oshrey, *J. Amer. Chem. Soc.*, 1950, **72**, 2844), $(M/d)^{25} = 18{\cdot}07$ c.c. (I.C.T., III, 25), distortion polarisation = 4·03 c.c. (Stranathan, *Phys. Review*, 1935, **48**, 538), $(n^2_D)^{25} = 1{\cdot}7756$ (I.C.T., VII, 13), $(n^2_{eff.})^{25} =$

1·86; and $A : B : C = 2·73 : 3·35 : 2·44$ (Angyal and Le Fèvre, *J.*, 1952, 1651); accordingly $_{T}P_{liq.} = 17·40$ c.c., whence $\mu_{liq.} = 0·808$ D.

Appropriate substitutions in equations (5), (6), and (7) yield values for $(\mu_{gas})_{calc.}$ of 1·37, 1·40, and 3·10 D, respectively, against 1·84 D by direct measurement (cf. Angyal and Le Fèvre, *loc. cit.*). Böttcher (*loc. cit.*) quotes also ε, d, and n^2_∞ for water at 100°; these by equations (5) or (7) lead to $(\mu_{gas})_{calc.} = 1·5$ or 3·0 D. It is seen that the predictions by (7) are some three times as high as those by (5) are low. Considering that between the H_2O molecules of water there are directed interactions of an exceptional kind (possibly producing pseudo-crystalline domains) not operative within organic liquids (for references, see Wells, "Structural Inorganic Chemistry," Oxford, 2nd Edn., 1950, pp. 427—432), we may claim that the applicability of equation (5) is not unsatisfactory. It is interesting that the abnormalities of physical properties shown by water do not occur with hydrogen sulphide, the dielectric constant of which according to Eversheim (*Ann. Physik*, 1904, **13**, 492) is 5·4 at 25° (measured under pressure). This value in conjunction with other quantities cited by Angyal and Le Fèvre (*loc. cit.*) yielded by equation (6) $(\mu_{gas})_{calc.} = 0·92$ D. The experimental figure is 0·89 D. Equation (7) with the same data gives $(\mu_{gas})_{calc.} = 0·95$ D.

[*Added, April 8th*, 1952.] Since the above paper was submitted, Everard, Kuman, and Sutton (*J.*, 1951, 2807) have redetermined $\mu_{C_6H_5}$ for $C_6H_5·CN$ at 25° as 4·05 D. By using this figure in lieu of the 3·74—3·97 D given in Table 1, the following values for μ_{gas} are obtained:

By (1)	By (2)	By (3)	By (4)
4·43	4·41	4·41	4·80

The forecasts by (2) and (3) are seen to agree well with $\mu_{gas(obs.)}$, *viz.*, 4·39 D (cf. Table 2).

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, November 5th*, 1951.]

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359. *The Chemistry of Ethylene Oxide. Part IV.* The Kinetics of the Reaction of Ethylene Oxide in Pyridine Solutions of Hydrogen Halides.*

By A. M. EASTHAM.

Ethylene oxide reacts with pyridine solutions of hydrogen halides to yield halogenohydrin and 2′-hydroxyethylpyridinium halide. A kinetic investigation of the reaction at 25° indicates that the dependence of the rate upon acid concentration decreases from second order to first order as the acid concentration increases, while simultaneously the proportion of halogenohydrin in the product increases. The change in order is attributed to a change in mechanism due to the association of the ions to form ion-pairs. The mechanism based on ion-pairs will also account for the facts that acids such as perchloric and nitric do not have identical catalytic activity in pyridine solutions and that in mixtures of acids the acids behave independently.

Studies of hydrogen chloride–lithium chloride solutions suggest that these two chlorides catalyse the reaction of ethylene oxide with pyridine in essentially similar fashion. The rate constant for hydrogen chloride is about seven times that for lithium chloride.

IN previous papers we reported the results of studies on the reaction of ethylene oxide with amines in aqueous and in pyridine solutions (Eastham, Darwent, and Beaubien, *Canadian J. Chem.*, 1951, **29**, 575, 585). Although the reaction takes the general form

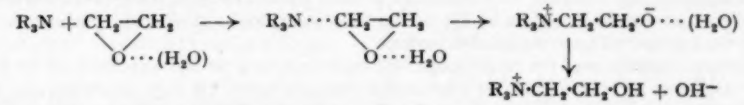
$$R_3N + CH_2{-}CH_2 + H^+ \longrightarrow R_3N^+·CH_2·CH_2·OH$$
$$\qquad\qquad\quad \backslash\,/ \qquad\qquad\qquad\quad$$
$$\qquad\qquad\quad O \qquad\qquad\qquad\quad$$

it was found to be independent of the proton source over the pH range 4—14 in aqueous solutions containing ammonium-type ions. No specific hydrogen-ion-catalysed reaction

* Part III, *Canad. J. Chem.*, 1951, **29**, 585.

was observed although from analogy with other ethylene oxide reactions one would be expected; our failure to find it was perhaps due to the fact that appreciable concentrations of both hydrogen ion and free amine cannot be obtained in the same solution.

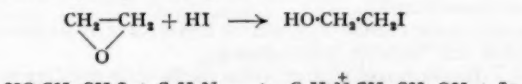
The results of the experiments in aqueous solution seem to indicate that water, through hydrogen bonding and/or solvation, plays an important part in the reaction and suggests a mechanism of the following type,



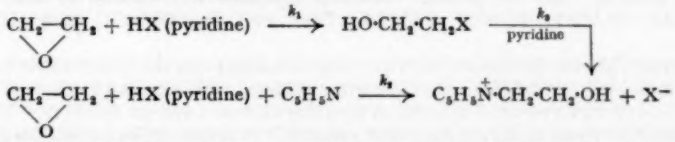
in which the rate-controlling step, the rupture of the C–O bond, is essentially an ionization process. Such an ionization would be assisted on the one hand by the high dielectric constant and solvating activity of water (cf. Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185), and on the other by the ability of nitrogen to form a positive ion.

In anhydrous pyridine solution, with pyridine acting as both solvent and reactant, the reaction was found to be strictly dependent upon the hydrogen-ion concentration, a fact readily explained on the basis of the above mechanism. More difficult to interpret, however, was the observation that when the hydrogen ion was supplied as the pyridinium salt of a strong acid the reaction rate was, qualitatively, proportional to the strength of the undissociated acid; for instance, perchloric acid was about twice as effective as sulphuric and three times as effective as nitric acid in promoting the reaction. Now in a solvent as basic as pyridine, where complete ionization of strong acids must be assumed, the proton source in all cases is presumably the pyridinium ion and therefore the acid anion must either modify the pyridinium ion or else must participate directly in the reaction mechanism. The latter alternative seemed unlikely since the addition of sodium perchlorate to the perchloric acid-catalysed reaction had no effect upon the rate, and we therefore concluded that the anion must influence proton availability.

However, it was also observed that when hydrogen iodide was employed as the proton source, the reaction occurred, at least in part, in two quite definite steps, which could be represented by the following simplified equations:



The final product, like that obtained from perchloric acid, is a 2′-hydroxyethylpyridinium salt but its formation in this case involves participation of an anion in the reaction mechanism. It seems unlikely that such participation occurs in the case of the perchlorate ion, and therefore in the presence of halogen acids two separate reactions must lead to the formation of the 2′-hydroxyethylpyridinium salts, *i.e.*,



In the case of hydrochloric acid k_3 is relatively small, and both primary processes may therefore be investigated by following simultaneously the disappearance of hydrogen and chloride ions. A study of these reactions was therefore undertaken with the object of obtaining further information on the reaction mechanism, particularly with respect to the role of the anion.

Experimental

Materials.—(a) *Pyridine.* Both fresh and recovered pyridine were employed and were prepared for use in the following manner. The pyridine was kept for several days over solid potassium hydroxide, then refluxed for a few hours and distilled. The distillate was carefully

fractionated to remove most of the remaining water and other low-boiling materials and kept for a day or two with anhydrous aluminium chloride. It was distilled from the aluminium chloride and, finally, carefully fractionated.

(b) *Pyridinium halides.* Pyridinium iodide and bromide were prepared as the crystalline salts by neutralizing the corresponding acids with pyridine and isolating and recrystallizing the products. The bromide was rather hygroscopic but was readily dried at 100°. The dry salts were analysed by titration with standard sodium hydroxide to a potentiometric end-point and found to contain not less than 99·7% of the theoretical amount of acid. Solutions of these salts were then prepared from weighed samples.

Pyridinium chloride was too hygroscopic for easy handling so was prepared as its pyridine solution. Gaseous hydrogen chloride was passed through sulphuric acid scrubbers and the dry gas absorbed in pyridine (solubility about 7 g./l.). The concentration of the solution was then determined by titration as described below.

Analyses.—Reaction mixtures were prepared and sampled as described in Part III (*loc. cit.*) and analysed according to the following procedure. A sample (10—50 c.c., but preferably about 20 c.c.) was transferred to a 125-c.c. long-necked flask and connected to a vacuum system by a ground-glass joint. The pressure was rapidly reduced to about 1 mm. and the time recorded at the onset of rapid ebullition, as most, if not all, of the ethylene oxide is removed at this point. The sample was then evaporated just to dryness at temperatures below 30°. Great care was necessary in evaporating the bromide solutions for the pyridinium bromide forms a flaky residue which may be carried through the long neck. Best results were obtained by shaking the flask so as to keep the precipitate wet until most of the pyridine had been removed.

The dry residue was taken up in about 25 c.c. of carbon dioxide-free water and titrated with carbonate-free alkali, the end-point being determined potentiometrically. The normality of the alkali was usually such that 5—6 c.c. were required for a sample at zero time and the titrations were reproducible and accurate to about $0 \pm 0{\cdot}02$ c.c. even with acid solutions as dilute as 0·001M. With very dilute solutions good end-points were obtained only when all excess of pyridine had been carefully removed from the sample.

On completion of the acid–base titration, the free pyridine in the solution was neutralized by adding 0·5M-perchloric acid to a pH of 3·8—4·0. The chloride ion was then determined by titration with standard silver nitrate solution by use of dichlorofluorescein (Kolthoff, Lauer, and Sunde, *J. Amer. Chem. Soc.*, 1929, **51**, 3273). The error in this titration was about 1% and on solutions of hydrogen chloride or hydrogen bromide the results were in excellent agreement with those obtained by acid–base titration.

The methods of analysis were tested on synthetic mixtures of hydrogen chloride and ethylene chlorohydrin in pyridine and found to be satisfactory.

Reaction Products.—In the reaction of ethylene oxide with pyridine solutions of hydrogen chloride, two principal products are formed, ethylene chlorohydrin and 2′-hydroxyethylpyridinium chloride: the latter is precipitated as a white crystalline salt at rather low concentrations and reactions cannot therefore be carried very far. The corresponding bromide and iodide are more soluble.

The crystalline product from a number of reactions was accumulated and washed thoroughly with pyridine. It was taken up in a minimum quantity of absolute methanol, the solution diluted with pyridine, and the product slowly precipitated with dioxan as fine, needle-like crystals (Found: C, 52·7; H, 6·07; Cl, 22·1. Calc. for $C_7H_{10}ONCl$: C, 52·6; H, 6·28; Cl, 22·2%).

Since ethylene chlorohydrin reacts with pyridine on heating and therefore cannot be separated by distillation, it was identified in the following manner. An excess of ethylene oxide was added to 50 c.c. of 0·18N-hydrogen chloride in pyridine and set aside for 24 hours. The mixture was then distilled at room temperature under vacuum. A small fore-run containing unreacted ethylene oxide was discarded, and the remainder collected at −70° with precautions to prevent the condensation of moisture in the solution. The distillate was then treated with sufficient α-naphthyl *iso*cyanate to react with all the chlorohydrin and kept for sixteen hours. A small precipitate of di-α-naphthylurea was filtered off, and the solution evaporated to dryness under vacuum. The residue was taken up in boiling hexane, and the solution filtered, concentrated, and cooled. The thread-like crystals which separated were shown by mixed m. p. determination to be identical with the urethane prepared from pure chlorohydrin; the yield of crude product was 1·2 g. (50% based on hydrogen chloride), and the m. p. 95—98°, and 99—100° after recrystallization from hexane.

Reaction of Ethylene Chlorohydrin with Pyridine.—An estimate of the rate at which ethylene

chlorohydrin is converted into 2′-hydroxyethylpyridinium chloride was obtained by preparing solutions of the chlorohydrin in pyridine and determining the rate of formation of chloride

TABLE 1.

Acid	Oxide							
0·0353 HCl	0·0565	Reaction, %	10	15	19	22	27	32
		Chlorohydrin, %	74	65	65	68	65	63
		10^3k	11·9	12·2	12·2	12·1	12·2	12·0
0·0685 HCl	0·0685	Reaction, %	16	21	28	36		
		Chlorohydrin, %	66	66	68	67		
		10^3k	13·3	13·3	13·3	13·4		
0·00919 HBr	0·0263	Reaction, %	24	38	46	54	67	
		Bromohydrin, %	77	81	80	78	71	
		10^3k	79·4	78·8	78·7	77·0	77·1	
0·0506 HBr	0·0682	Reaction, %	23	40	55	63		
		Bromohydrin, %	90	89	84	81		
		10^3k	83·2	81·2	81·2	81·0		
		Reaction, %	25	40	55	65	75	
0·00385 HI	0·0239	10^3k	195	189	192	188	187	
0·00977 HI	0·0283	,,	227	222	—	218	214	
0·0604 HI	0·0602	,,	255	253	249	—	248	

ion. The first-order rate constant thus obtained was approximately 3×10^{-5} min.$^{-1}$ at 25°, a value too low to have any significant effect on the composition of the reaction products. This constant was not influenced by addition of small amounts of hydrogen chloride.

Data.—All experiments were performed at 25·0° in a bath controlled to 0·005°. All rate constants recorded, unless otherwise stated, are second-order constants expressed as

FIG. 1.

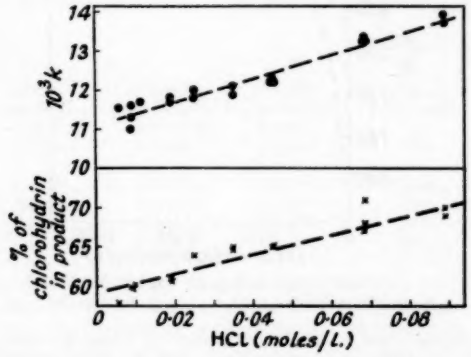
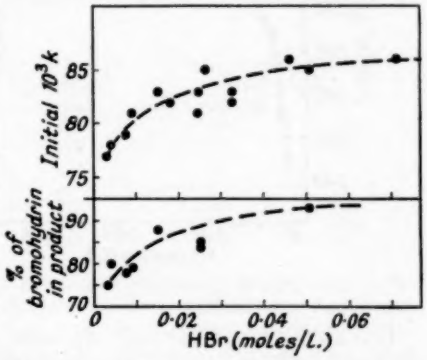


FIG. 2.



mole^{-1} l. min.$^{-1}$ and calculated from the expression $d[\text{products}]/dt = k[\text{oxide}][\text{acid}]$ on the assumptions that one molecule of oxide disappears with one molecule of acid, and that $k = k_1 + k_2$.

For the hydrogen chloride reactions where no deviations from second order were observed, the rate constants were obtained in the usual way by plotting the data and obtaining the best straight line through the points. With the bromide, and more especially with the iodide, where deviations from second order were observed, the rate constants were calculated for each point and plotted against the percentage reaction. The initial rate was then estimated by extrapolation to zero reaction. Some typical runs for each acid are shown in Table 1, where concentrations of acids and of ethylene oxide are given in moles/l.

Results.—The data for the reaction of ethylene oxide in pyridine solutions of hydrogen chloride are shown in Table 2 and Fig. 1. They are perhaps somewhat more accurate than the corresponding data for the bromide and iodide because, experimentally, the individual chloride reactions follow a strict second-order course and because chlorohydrin is relatively stable in pyridine. Actually, since the rate constant shows an increase with increasing hydrogen chloride concentration, deviations from second order might be expected but none was observed, probably because the precipitation of 2′-hydroxyethylpyridinium chloride prevented the reactions being

carried beyond about 40% conversion. The percentage of chlorohydrin in the reaction product remained constant, within experimental error, over the course of the run.

TABLE 2.

HCl (in moles/l.)	Oxide (in moles/l.)	10^3k*	Chlorohydrin in product, %	HCl (in moles/l.)	Oxide (in moles/l.)	10^3k*	Chlorohydrin in product, %
0·1115	0·1355	14·4	—	0·0353	0·0565	12·1	65
,,	0·0892	14·2	72	,,	0·0562	11·9	65
0·0890	0·0766	13·9	69	0·0187	0·0565	11·7	61
,,	0·0674	(13·7)	70	,,	0·0377	11·8	61
0·0685	0·0910	13·3	67	0·0113	0·0487	11·7	—
,,	0·0692	13·3	71	0·00915	0·0367	11·6	60
,,	0·0444	13·3	68	,,	0·0232	11·3	60
0·0447	0·0791	12·2	65	0·00880	0·0334	11·0	60
,,	0·0533	12·2	65				
,,	0·0277	12·3	(63)				

* In l. mol.$^{-1}$ min.$^{-1}$.

The data for the reactions with hydrogen bromide and iodide are shown in Figs. 2 and 3. No attempt was made to determine iodohydrin because it reacts rapidly with pyridine; for the same reason the bromohydrin determinations may be slightly low.

FIG. 3.

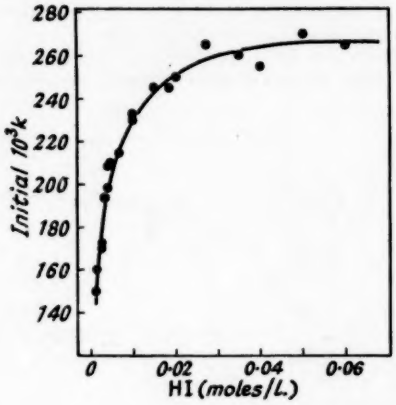
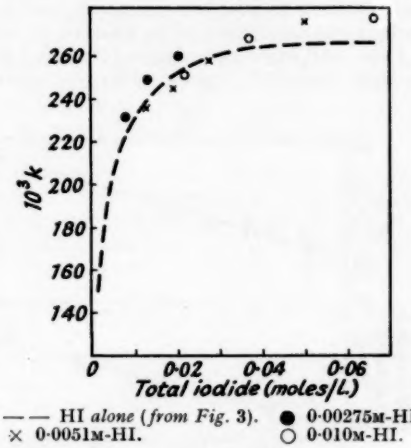


FIG. 4.



It is apparent that the strict first-order dependence on acid concentration observed with perchloric and other " inert " acids has given way in the case of halogen acids to a dependence which seems to decrease from second to first order as the acid concentration is increased. The interpretation of this change in order obviously requires further information on the effect of (*a*) halide ions and (*b*) ionic strength on the reaction rate.

The only alkali halides readily soluble in pyridine are the lithium salts and sodium iodide. Unfortunately, however, the addition of lithium chloride to hydrogen chloride solutions gave rates which suggested that the lithium ion behaved like a proton, and the study of halide-ion effects was therefore restricted to the sodium iodide–hydrogen iodide system. The results with lithium chloride are considered separately (see p. 1943).

In Fig. 4, the observed second-order rate constants, calculated from the disappearance of *acid* in the solution, are plotted against the total iodide-ion concentration for various mixtures of sodium iodide and hydrogen iodide. It is seen that k varies with the total iodide rather than with the hydrogen iodide concentration and it is therefore not surprising that the deviations from second order (Table 1) almost disappear in the presence of relatively large amounts of sodium iodide, since under these conditions the iodide-ion concentration remains essentially constant throughout the reaction.

The increase in the rate constant thus seems to be related either to the iodide-ion concentration or to the ionic strength. The investigation of ionic strength effects in solvents

of low dielectric constant, however, is difficult, apparently because the reactive entities are not ions, but ion-pairs. For example, when sodium perchlorate is added to a pyridine solution of hydrogen iodide, an equilibrium between ion pairs is set up: $C_5H_5N,HI + NaClO_4 \rightleftharpoons NaI + C_5H_5N,HClO_4$, and our evidence suggests that such equilibria move in the direction which favours the association of the smallest negative with the smallest positive ion (Eastham and Jeffrey, unpublished). Now the total iodide-ion concentration in the solution remains unchanged as a result of the above equilibrium, and hence from the point of view of the data of Fig. 4, the significant change is the substitution of perchloric acid for a part of the hydriodic acid. Perchloric acid is, however, at least as strong an acid as hydriodic and one might therefore expect that the rate of disappearance of ethylene oxide would be, if anything, increased by the addition of sodium perchlorate. Actually, however, the rate was very sharply decreased, which leads to the conclusion that the hydriodic and perchloric acids act independently according to their individual rate constants of 200×10^{-3} and 24×10^{-3}, respectively.

It is evident, then, that in such solutions there are no "neutral" salts and hence that salt effects cannot be investigated directly. It seemed possible, however, that by studying mixtures of acids one might be able to obtain some information both on ionic-strength effects and on the extent of independent behaviour of acids. Rate studies were therefore made on solutions containing mixtures of hydriodic and perchloric acids and hydriodic and nitric acids, in the presence of excess of ethylene oxide. Now if the two acids behave independently, the contribution of the nitric or perchloric acid to the overall rate will be small, and may be estimated fairly accurately from the respective rate constants, $7{\cdot}41 \times 10^{-3}$ and $23{\cdot}9 \times 10^{-3}$; the contribution of the hydrogen iodide may then be obtained and should yield a rate constant corresponding to a value obtained from Fig. 3 either at the same iodide concentration or at the same ionic strength. Measurements were made in the initial stages of reaction only, in order to simplify the calculations and to minimize the introduction of new ionic equilibria by the 2′-hydroxyethylpyridinium salts formed during the reaction. The results of these experiments are shown in Table 3. The results for mixtures of nitric and hydriodic acids are evidently in

TABLE 3.

HI (moles/l.)	HNO_3 (moles/l.)	Oxide (moles/l.)	$10^3k_{HNO_3}$ (assumed)	10^3k_{HI} (obs.)	10_3k_{HI} from Fig. 3 at equivalent ionic strength	$[I^-]$
0·00356	0·00376	0·0311	7·4	197	222	192
0·00354	0·00366	0·0262	7·4	190	219	190
HI	$HClO_4$	Oxide	$10^3k_{HClO_4}$			
0·00331	0·00255	0·0362	23·9	232	210	188
0·00371	0·00344	0·0305	23·9	241	218	195
0·00385	0·00495	0·0305	23·9	228	225	195

excellent agreement with the view that the rate of the iodide reaction is determined by the iodide-ion concentration rather than by the ionic strength, but unfortunately the results with perchloric acid fail to confirm them. It does seem clear, however, that the acids act essentially independently of each other, and hence that the reactive species are ion-pairs, or some other associated form of the acid.

DISCUSSION

A mechanism of the type

$$\text{Oxide} + H^+ \rightleftharpoons \text{Oxide},H^+ \quad (a)$$

$$\text{Oxide},H^+ + I^- \longrightarrow HO{\cdot}CH_2{\cdot}CH_2I \quad (b_1)$$

or

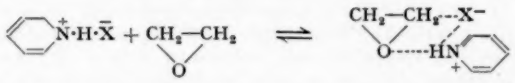
$$\text{Oxide},H^+ + C_5H_5N \longrightarrow HO{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5 \quad (b_2)$$

has been suggested by King, Berst, and Hayes (*J. Amer. Chem. Soc.*, 1949, **71**, 3498) to explain the formation of 2′-hydroxyethylpyridinium salts in pyridine solutions of hydrogen iodide; it is basically similar to the type of mechanism usually postulated for the reactions of ethylene oxide in aqueous solutions (Hammett, "Physical Organic Chemistry," McGraw-Hill, 1940). Such a mechanism would account for the shape of the curves in Figs. 3 and 4 if, with increasing iodide-ion concentration, step (b_1) becomes relatively very rapid so that the rate-controlling step shifts from (b) to (a). The dependence of the rate of

process (b_2) upon the acid strength of the anion would then have to be attributed to a variation in the equilibrium constant of step (*a*), *i.e.*, a sort of general acid catalysis, but (see also Part III, *loc. cit.*) this view is not without objections, the most serious being that it does not permit an explanation of the independent behaviour of acids in mixtures, or of the marked decrease in rate which occurs when sodium perchlorate is added to a pyridine solution of hydrogen iodide. In addition, it may be noted that on the basis of this mechanism it is merely fortuitous if the reaction acquires second-order kinetics at the point where halogenohydrin becomes the exclusive product of the reaction.

It seems therefore that the mechanism as written can hold only for those very dilute solutions where dissociation into individual ions is high and where, experimentally, the reaction shows third-order kinetics. It can, however, be modified to cover most of the experimental data if one supposes that the change in kinetic order with increasing halide-ion concentration reflects not so much a change in mechanism as a change in the ionic character of the solutions. The fully ionic mechanism (above) then gives way at higher concentrations to a mechanism in which the kinetic entities are not ions, but ion-pairs.

The first step in such a mechanism would be the rapid formation of a complex :



Reaction would then proceed through the slow decomposition of this complex either by rearrangement to halogenohydrin or by attack of solvent molecules at carbon, both processes being experimentally of the second order. The essential change which takes place with increasing concentration is thus presumed to be a closer association of the anion with the complex.

It seems necessary to suppose that an electrostatic association exists between the carbon and the anion, which so disturbs the polarity or resonance of the oxide ring that the susceptibility of the oxide to solvent attack is altered. This assumption follows from the fact that it is the basicity rather than the size of the anion which determines the rate, and hence that the effect is electronic rather than steric.

If this hypothesis is correct, then at some low concentration where dissociation of the ions is complete, the formation of 2′-hydroxyethylpyridinium salts should occur at identical rates with all strong non-nucleophilic acids. Little evidence is available on this point but it was noted in the earlier work that the rates with sulphonic acids do seem to show an upward trend at low concentrations whereas those with nitric acid do not. Since dissociation effects would be greatest with the largest ions, these very incomplete data may provide some support for our view.

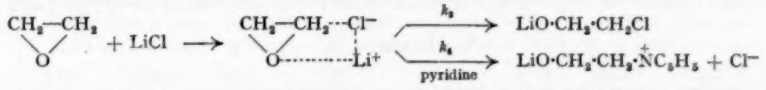
The close association between the anion and carbon, as postulated above, would be expected to increase the rate of nucleophilic attack by the ion and to lead to a maximum rate when association of the ions is complete. With active ions such as bromide and iodide this region of maximum rate should also be a region of almost exclusive halogenohydrin formation, as is observed. With the less active chloride ion one might expect both the rate and the ratio of products to be constant over the whole experimental range, since chlorides dissociate less readily than do the bromides and iodides. In practice, however, as the chloride-ion concentration is increased, both the rate and the proportion of chlorohydrin in the product increase slowly. No satisfactory explanation for this rise has been obtained.

Some support for the views expressed here can be obtained from the dissociation constants of alkali iodides in pyridine solutions at 25° (Burgess and Kraus, *J. Amer. Chem. Soc.*, 1948, **70**, 706), since the evidence suggests that pyridinium and sodium salts are not greatly different in their dissociations. From the constant it may be estimated that sodium iodide is about 25% dissociated at 0·001M-, and 10% at 0·01M-concentration; the levelling off of the curve in Fig. 3 at about 0·03M is therefore in good agreement with these data. It follows that the effect of sodium iodide on the rate (Fig. 4) can be readily interpreted as a common-ion effect.

Also relevant is the work of Walvekar, Phalnikar, and Bhide (*J. Indian Chem. Soc.*, **1943**, **20**, 131) on the fission of aromatic ethers by halogen acids. These authors report that cleavage of the ethers by un-ionized acids in carbon tetrachloride solution is very slow, but is greatly accelerated by the addition of a small amount of pyridine.

Catalysis of the Reaction of Ethylene Oxide with Hydrogen Chloride by Lithium Chloride.— In an effort to determine whether the increase in the rate of reaction described on p. 1939 was due to the increase in chloride-ion concentration, lithium chloride was added to the reaction mixtures, and the rate of acid disappearance determined. It was found that the rate constant, calculated on the assumption of first-order dependence on both acid and oxide, increased steadily throughout the reaction; the deviation was most marked at high ratios of lithium chloride to hydrogen chloride. This behaviour was in distinct contrast to the effect of sodium iodide on the reaction of ethylene oxide with hydrogen iodide, for there the sodium iodide, apparently by maintaining a relatively constant concentration of iodide ion, had the effect of suppressing deviations from second order.

The results suggested that the lithium chloride was participating directly in the reaction. Now it is known (Rheinbodt, Luyken, and Schmittmann, *J. pr. Chem.*, **1937**, **148**, 81) that lithium halides, in contrast to the alkali and ammonium halides, form stable oxonium compounds with dioxan. The ethylene oxide molecule in all probability is structurally quite similar to dioxan, and might therefore form similar complexes, which in turn would presumably resemble the ethylene oxide–pyridinium salt complexes postulated earlier as the reactive intermediates in the reaction between oxide and acids. We may therefore consider the possibility of a reaction of the following form:



Such a mechanism is exactly analogous to that postulated earlier but in the presence of hydrogen chloride would be followed immediately by a rapid exchange reaction, *i.e.*,

$$\mathrm{LiO{\cdot}CH_2{\cdot}CH_2X + HCl \longrightarrow HO{\cdot}CH_2{\cdot}CH_2X + LiCl}$$

The net effect therefore would be a more rapid disappearance of both oxide and acid, in agreement with the experimental data.

On this basis we may set up the following rate expression for the reaction,

$$\mathrm{d[products]}/dt = k_5[\mathrm{oxide}][\mathrm{HCl}] + k_6[\mathrm{oxide}][\mathrm{LiCl}]$$

If a, b, and c are the initial concentrations of oxide, acid, and lithium chloride, respectively, and if x and y are the amounts of oxide disappearing, in time t, by the respective mechanisms, then

$$\mathrm{d}(x+y)/\mathrm{d}t = k_5(a-x-y)(b-x-y) + k_6(a-x-y)c$$

which on integration gives, when $x + y = z$ and $k_5b + k_6x = p$,

$$t = \frac{2{\cdot}303}{p - ak_5} \log \frac{a(p - k_5z)}{p(a - z)}$$

Since z is the acid consumed, it can be determined and we have therefore an expression which should yield values of k_6, provided that the values of k_5 previously determined (Fig. 1) can be applied. The constancy of k_6 will be a test of the mechanism.

In practice, the solution of this equation was somewhat difficult and we therefore adopted the following rather laborious procedure. The equation was rearranged to

$$\frac{k_6c + k_5(b-a)}{2{\cdot}303}\, t = \log \frac{a}{k_6c + k_5b} \cdot \frac{k_6c + k_5(b-z)}{a - z}$$

and the known values of k_5, a, b, and c were substituted. Then for each experimental value of z and t a series of arbitrary values of k_6 was introduced and the numerical values of each side of the equation were plotted against k_6. Two curves were thus obtained which at their intersection gave the desired value of k_6.

From the results of the experiments with sodium iodide–hydrogen iodide systems, it would appear that k_5 should be assigned a value corresponding to the equivalent chloride-ion concentration (hydrogen chloride plus lithium chloride) rather than to the hydrogen chloride concentration. However, as was pointed out earlier, the increase in rate with increasing hydrogen chloride occurs to a large extent in the region where ionic dissociation should be small, and where the chlorohydrin in the reaction product is still increasing. Accordingly, the data were calculated for both possible values of k_5. It was found that the value of k_5 obtained at equivalent chloride-ion concentration gave values of k_6 which increased steadily throughout the individual runs, whereas the value of k_5 obtained at equivalent hydrogen chloride concentration gave values of k_6 which were not only constant between runs but were reasonably constant throughout the individual runs, from 20% to 70% conversion.

The range of concentrations over which the equation can be tested is rather limited for a number of reasons. First, the presence of lithium chloride makes difficult the removal of the last traces of pyridine, with the result that the end-point for the acid–base titration is less sharp and very low concentrations cannot be examined. For the same reason the silver nitrate titrations lead to somewhat low values for the percentage of chlorohydrin in the reaction product; it appears that, in general, the proportion of chlorohydrin formed is not greatly changed by the addition of lithium chloride. Secondly, the low value of k_6 relative to k_5 makes necessary a high ratio of lithium chloride to hydrogen chloride in order that the lithium contribution to the overall rate may be determined with some degree of accuracy. Other restrictions are imposed by the form of the integrated equation above. Within these limits, the reaction has been examined with the results shown in Table 4.

TABLE 4.*

HCl	LiCl	Oxide	10^3k_5	10^3k_6	HCl	LiCl	Oxide	10^3k_5	10^3k_6
0·00624	0·0218	0·01715	11·3	1·42	0·01345	0·0613	0·0470	11·6	1·46
0·00624	0·0218	0·0308	11·3	1·42	0·01345	0·0613	0·0346	11·6	1·44
0·00876	0·1046	0·0320	11·4	1·45	0·0210	0·0382	0·0352	11·75	1·30
0·00876	0·0523	0·0323	11·4	1·37	0·0210	0·0382	0·0450	11·75	1·25
0·00876	0·0261	0·0294	11·4	1·44	0·0210	0·0546	0·0335	11·75	1·41
0·00876	0·0105	0·0326	11·4	1·20 [a]	0·0210	0·0546	0·0439	11·75	1·39
0·00957	0·0335	0·0532	11·5	1·50	0·0222	0·0669	0·0387	11·8	1·44
0·00957	0·0335	0·0401	11·5	1·52	0·0222	0·0669	0·0337	11·8	1·40
0·0105	0·0942	0·0314	11·5	1·47	0·0353	0·0623	0·0502	12·0	1·43 [b]
0·0105	0·0471	0·0310	11·5	1·42	0·0353	0·0468	0·0507	12·0	1·30

* Concentrations in moles/l.; k_5 and k_6 in l. mole^{-1} min.$^{-1}$. Chlorohydrin (%): (*a*) 57; (*b*) 60.

It is evident from the data of Table 4 that, within the limits of concentration reported here, the reaction rate seems to be expressed reasonably well by the expression

$$\mathrm{d[product]/d}t = k_5[\mathrm{oxide}][\mathrm{HCl}] + 1{\cdot}4 \times 10^{-3}[\mathrm{oxide}][\mathrm{LiCl}]$$

when k_5 is assigned a value obtained from Fig. 1 at equivalent hydrogen chloride concentration. It should be noted, however, that the integrated rate expression is not sufficiently sensitive to small fluctuations in k_6 to permit any very definite conclusions. In practice, excellent results are obtained when the initial mol.-ratio of lithium chloride to hydrogen chloride is at least three to one, since under these conditions k_6 makes an appreciable contribution to the overall rate, particularly in the advanced stages of the reaction. However, with low lithium chloride/hydrogen chloride ratios the value of k_6 in the initial stages of the reaction is usually low and rises steadily as the reaction proceeds. The following typical values of 10^3k_6 illustrate this point (concentrations are given in moles/l.):

			Reaction, %			
HCl	LiCl	Oxide	15 min.	25 min.	45 min.	55 min.
0·00624	0·0218	0·01715	1·35	1·46	1·40	1·46
0·0203	0·0382	0·0450	1·08	1·18	1·37	1·38

The low values are always obtained under conditions which lead to the greatest experimental error and it is therefore not possible to assess their significance.

The foregoing data, then, seem to indicate that lithium salts, like acids, will promote the reaction of ethylene oxide with pyridine. Qualitative support for this view is obtained from the observation that pyridine solutions of ethylene oxides rapidly turn brown on addition of lithium perchlorate, owing in all probability to the formation of degradation products of 2′-hydroxyethylpyridinium hydroxide. The instability of these pyridinium bases will probably prevent a study of catalysis by lithium salts alone in pyridine solutions, but it may be possible to demonstrate such catalysis in solutions of primary or secondary amines where the reaction involves a simple proton transfer and not proton consumption.

Applied Chemistry Division, National Research Council,
Ottawa, Canada. [*Received, September 24th*, 1951.]

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360. *Reactions with Periodate of* 2 : 3 : 4 : 6-*Tetramethyl* D-*Glucose, the Trimethyl* D-*Glucopyranoses, and Other Methoxy-compounds.*

By G. D. Greville and D. H. Northcote.

Reactions of all four trimethyl D-glucopyranoses with metaperiodate at pH 5 have been studied; 3 : 4 : 6-trimethyl glucose can be determined in presence of the others since it alone yields volatile acid (one equivalent). Unexpectedly, 2 : 3 : 6-trimethyl and 3 : 4-dimethyl D-glucose resist attack by metaperiodate at $C_{(3)}$ and the adjacent unmethylated carbon atom.

In carbohydrate derivatives periodate reacts with (i) α-glycol groups, (ii) active hydrogen groups, (iii) some structures lacking (i) (actual or potential) and (ii). Type (iii) reactions with some methylated carbohydrate derivatives have been studied. They occur at pH 7·5 but only very slowly at pH 5; they are not dependent on hydroxyl groups, and their rate increases with the number of methoxyl groups. Not all methoxy-compounds react at pH 7·5.

2 : 3 : 4-Trimethyl D-glucose, purified chromatographically, had $[\alpha]_D^{20}$ +78·7° in water, 10° higher than any previously recorded value.

Reactions with periodate have become important in analyses of polysaccharides and methylated monosaccharides obtained from them. The reactions with many of the latter have been insufficiently studied; investigations on D-glucose derivatives are reported here. Rates of reaction of periodate and the nature of the products depend on pH. Many methylated monosaccharides fail to give the expected amount of formaldehyde with periodic acid, but the yield is increased with periodate buffered at pH 7·5 (Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476; Jeanloz, *Helv. Chim. Acta*, 1944, **27**, 1509; Bell, *J.*, 1948, 992; Bell, Palmer, and Johns, *J.*, 1949, 1536). The periodate consumption then exceeds, often greatly, that required by the α-glycol groupings (" over-consumption ") (Bell *et al.*, *loc. cit.*; Bell and Greville, *J.*, 1950, 1902). Thus the increased formaldehyde production accompanies, and probably depends upon, attack on groups other than the primary alcohol group and its neighbour; and, in general, periodate at pH 7—8 attacks parts of the molecule lacking hydroxyl groups owing to methylation or glycoside formation (Grangaard, Gladding, and Purves, *Paper Trade J.*, 1942, **115**, No. 7, 41; also Jeanloz and Forchielli, *Helv. Chim. Acta*, 1950, **33**, 1690; *J. Biol. Chem.*, 1951, **188**, 361; **190**, 537). Demethylation or cleavage of the chain may well occur.

It is thus convenient to distinguish at least three types of reaction of periodate with carbohydrates and their derivatives: (i) Reactions with $-CH(OH)\cdot CH(OH)-$ and $-CH(OH)\cdot CO-$, $-CH(OH)\cdot CH(NH_2)-$, and related groups (" Malapradian reactions "). (ii) Oxidations at active hydrogen groups (Sprinson and Chargaff, *J. Biol. Chem.*, 1946, **164**, 433), *e.g.*, in structures left after Type (i) oxidations of hexofuranosides and uronides (Huebner, Lohmar, Dimler, Moore, and Link, *J. Biol. Chem.*, 1945, **159**, 503; Halsall, Hirst, and Jones, *J.*, 1947, 1427) and of maltose and amylose (Potter and Hassid, *J. Amer. Chem. Soc.*, 1948, **70**, 3488). (iii) Reactions with compounds, or parts of compounds,

lacking groupings involved in (i) and (ii), *e.g.*, methylated carbohydrate derivatives without actual or potential α-glycol structure [Type (ii) or (iii) reactions occurring with Type (i) have usually been designated " over-oxidation "].

We have studied at 22° (*a*) the reaction of metaperiodate (pH 5) with tri- and tetramethyl glucopyranoses, and (*b*) the occurrence and velocity, with various methylated derivatives, of Type (iii) reactions. It may be pointed out that precautions are usually taken to minimise Type (iii) reactions in analytical uses of periodate (Halsall *et al.*, *loc. cit.*; Potter and Hassid, *loc. cit.*). Certain terms used in this paper are thus defined:

" Metaperiodate ": aqueous $NaIO_4$ (pH 5).

" Neutral periodate ": aqueous periodate at pH 7·5—7·6.

" Moles of periodate ": moles of periodate per mole of sugar initially present.

" Volatile acid ": acid steam-distilled from solutions acidified with potassium hydrogen sulphate.

" Periodate consumed ": periodate disappearance measured solely by arsenite titration at pH 7·5.

Note. Hughes and Nevell (*Trans. Faraday Soc.*, 1948, **44**, 1941) found that metaperiodate reacting with glucose is partly converted, without reduction, into a form unreactive with arsenite in presence of sodium hydrogen carbonate.

Reactions with Metaperiodate.—With 2 : 3 : 6- and 2 : 4 : 6-trimethyl glucose only 0·05 mole of metaperiodate is consumed in 200 hours (Expt. 1). The low reactivity of the 2 : 3 : 6-compound has already been noted by Palmer (Thesis, Cambridge, 1951) with periodate in phosphate buffer pH 7·5. 2 : 3 : 4-Trimethyl glucose reacts more rapidly than the above two sugars, but still slowly (0·8 mole of metaperiodate in 200 hours) (Expt. 1). The progress of the reaction is similar to that noted in potassium phthalate buffer of pH 6 (Bell *et al.*, *loc. cit.*), but differs in that the periodate consumption goes beyond one mole. This difference may be due to the precipitation of potassium periodate by the buffer used by Bell *et al.* (cf. Halsall *et al.*, *loc. cit.*). 3 : 4 : 6-Trimethyl glucose rapidly consumes one mole of metaperiodate (unchanged up to 90 hours) (Expt. 2). One equivalent of a volatile acid, almost certainly formic, is found (Expt. 3). 2 : 3 : 4 : 6-Tetramethyl glucose unexpectedly consumes metaperiodate slightly faster than the 2 : 3 : 6- and the 2 : 4 : 6-analogue (Expt. 6).

The 3 : 4 : 6- and the 2 : 4 : 6-compound behave as expected. It is peculiar that 2 : 3 : 6-trimethyl glucose reacts no more rapidly than does the 2 : 4 : 6 isomer. In an aldohexose, carbon atom 5 will carry a hydroxyl group only when the sugar is in the aldehyde or the furanose form, and Jeanloz (*loc. cit.*) suggested that 2 : 3 : 4-trimethyl glucose reacts slowly with metaperiodate because it cannot assume the furanose configuration. A similar consideration may apply to 2 : 3 : 6-trimethyl glucose, which also can have an α-glycol structure only in the aldehyde form. Two compounds are known which, although they possess this structure, are unattacked; these are 1 : 6-anhydro-β-D-glucofuranose (Dimler, Davis, and Hilbert, *J. Amer. Chem. Soc.*, 1946, **68**, 1377) and 1 : 6-anhydro-α-D-galactofuranose (Alexander, Dimler, and Mehltretter, *ibid.*, 1951, **73**, 4658). This resistance was ascribed either to the *trans*-configuration of the hydroxyl groups or to the double lactol ring system. The former explanation is the less likely, since 1 : 6-anhydro-β-glucopyranose is attacked quite rapidly by metaperiodate (Jackson and Hudson, *J. Amer. Chem. Soc.*, 1940, **62**, 958; also see Expt. 8).

With 3 : 4-dimethyl glucose (Expts. 2 and 5), only one mole of metaperiodate is consumed, no formaldehyde appears, and one equivalent of volatile acid is found. The immunity of $C_{(5)}$ and $C_{(6)}$ may only partly be due to the impossibility of the sugar's assuming the furanose form, for when it has reacted, no titratable acid is present in the solution (also with 3 : 4 : 6-trimethyl glucose). Probably the reaction with metaperiodate yields a product still containing six carbon atoms:

3 : 4-Dimethyl glucose $\xrightarrow{NaIO_4}$ 6-carbon compound $\xrightarrow{H^+}$ $H{\cdot}CO_2H$ + (?) 2 : 3-dimethyl arabinose.

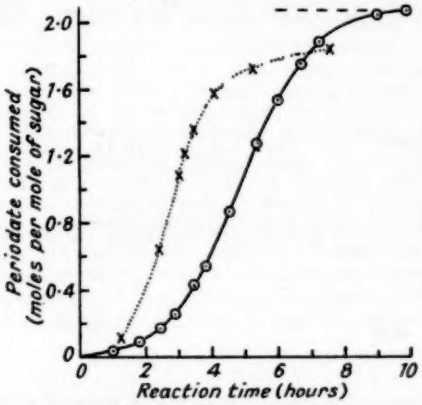
This will be the subject of a future communication. The product is rather stable in metaperiodate solution, and if it is the cyclic diester of periodic acid suggested by Criegee

(*Chem. Abs.*, 1935, **29**, 6820; see also Hughes and Nevell, *loc. cit.*) or, more likely, the formic ester (Halsall *et al.*, *loc. cit.*; Meyer and Rathgeb, *Helv. Chim. Acta*, 1949, **32**, 1102), there will be no adjacent hydroxyl group unless it breaks down. Even then the resulting dimethyl pentose is likely to be as resistant as 2 : 3 : 4-trimethyl glucose, since they have the same structure about their four highest-numbered carbon atoms.

The different behaviour of the four trimethyl glucopyranoses towards metaperiodate allows the 3 : 4 : 6-compound to be determined in the presence of the others by measurement of the volatile acid after 12 hours (Expt. 4). The method is still applicable after 60 hours' treatment. Previously, this sugar had been determined in presence of the others by weighing the hydrazodicarbonamide (Barker, Hirst, and Jones, *J.*, 1938, 1695; Granichstädten and Percival, *J.*, 1943, 54), and also by chromatographic separation of the *p*-phenylazobenzoyl derivatives of the glucitols (Boissonnas, *Helv. Chim. Acta*, 1947, **30**, 1689). The periodate method is simple and accurate.

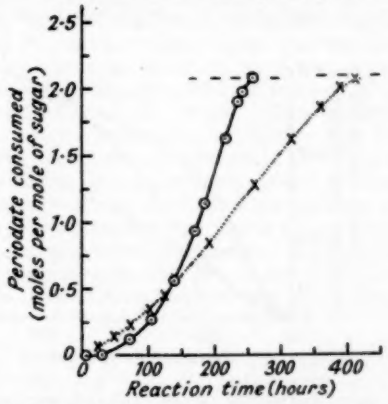
Reactions with Neutral Periodate.—In phosphate at pH 7·5, 2 : 3 : 6-trimethyl glucose is slowly attacked by periodate (1 mole in about 200 hours), consumption continuing to

FIG. 1. *2 : 3 : 4-Trimethyl glucose with 2·08 moles of periodate.*



⊙ *In phosphate*, pH 7·5 (*Expt.* 12).
× *Without buffer*, pH 7·6 (*Expt.* 18).

FIG. 2. *Reactions in phosphate*, pH 7·5.



⊙ *2 : 4 : 6-Trimethyl glucose with 2·09 moles of periodate* (*Expt.* 11).
× *2 : 3 : 6-Trimethyl glucose with 2·11 moles of periodate* (*Expt.* 10).

(*Horizontal broken lines show initial periodate.*)

3 moles or more (Fig. 2, Expt. 10). Since no break in the curve appears near one mole, the attack probably occurs simultaneously at several points. The 2 : 4 : 6-compound consumes periodate somewhat more rapidly (Fig. 2, Expt. 11). It is remarkable that this compound should react more rapidly than one with potential α-glycol structure. With 2 : 3 : 4 : 6-tetramethyl glucose there is a further increase in speed (1 mole in about 100 hours) (Expt. 14). With these compounds which are scarcely attacked by metaperiodate, the rate in phosphate at pH 7·5 is not even dependent on the number of actual or potential hydroxyl groups, but rather on the number of methoxyl radicals.

14 Moles of periodate are needed to oxidise tetramethyl glucose completely to formic acid, and 24 to carbon dioxide. Periodate consumption ceases when 14·5 have been used (Expt. 14). Some volatile acid (almost certainly formic) appears at first, but nearly disappears by the end of the reaction. With the corresponding glucoside the reaction is still continuing slowly when 15 moles of periodate have been consumed; very little volatile acid is then found (Expt. 15).

2 : 3 : 4-Trimethyl glucose reacts with metaperiodate considerably faster than the 2 : 3 : 6- or the 2 : 4 : 6-compound, and in phosphate the speed (1 mole in about 5 hours) is

also of a totally different magnitude (Fig. 1; cf. Bell *et al.*, *loc. cit.*). Type (iii) reactions may thus be as rapid as Type (i). There is no break in the curve near one mole, hence no preferential Type (i) attack at $C_{(3)}$ and $C_{(6)}$. This explains the appearance of formic acid together with less than one mole of formaldehyde (Bell *et al.*, *loc. cit.*). With 3 : 4 : 6-trimethyl glucose, the rapid disappearance of one mole of periodate is followed by a slower but steady consumption (Expt. 13, i), due only in minor degree to oxidation of the formic acid (Expts. 13, ii and 17). With 3 : 4-dimethyl glucose the second stage is more rapid (Expt. 13, iii; cf. Bell and Greville, *loc. cit.*). Since the intermediate compound already mentioned decomposes in a few hours, the *initial* oxidation of 3 : 4 : 6-trimethyl glucose should lead to 2 : 3 : 5-trimethyl arabinose, and that of 3 : 4-dimethyl glucose to 2 : 3-dimethyl arabinose. These products resemble, in distribution of methyl radicals, 2 : 4 : 6- and 2 : 3 : 4-trimethyl glucose, respectively. As the latter reacts much faster than the former, the more rapid second stage with 3 : 4-dimethyl glucose is understandable.

The presence of a free reducing group is not necessary for Type (iii) reactions, as is shown by 3 : 4-dimethyl, 3 : 4 : 6-trimethyl, and 2 : 3 : 4 : 6-tetramethyl β-methylglucosides (Expt. 15, i); the last-named has no hydroxyl group at all. Again, the rate of consumption of periodate increases with the number of methyl groups.

To test whether periodate in phosphate at pH 7·5 will attack any monomethyl α-glycol or simple methyl ether, 2-methoxyethanol and *n*-butyl methyl ether were chosen. Neither

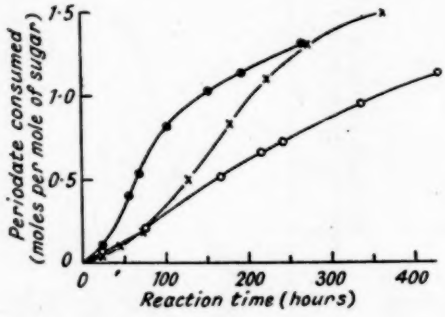


FIG. 3. *Reactions with periodate (2·1 moles) initially at* pH 7·6, *without buffer addition (Expts. 19, 20).*

○ 2 : 3 : 6-*Trimethyl glucose.*
× 2 : 4 : 6-*Trimethyl glucose.*
● 2 : 3 : 4 : 6-*Tetramethyl glucose.*

consumed periodate (Expt. 16). Even some methylated derivatives of monosaccharides do not react; *e.g.*, 2-benzoyl 3 : 4 : 6-trimethyl β-methylglucoside and 2 : 3 : 4-trimethyl 1 : 6-anhydro-β-glucose (Expt. 16). The 1 : 6-anhydro-ring is no bar to action of periodate on α-glycols, since 1 : 6-anhydro-β-glucopyranose reacts rapidly.

In no reaction, with or without phosphate, have we seen evidence of free iodine.

Most of these reactions in phosphate proceed with increasing velocity. For example (Figs. 1 and 2), the velocity increases until about two-thirds of the periodate have disappeared, and then decreases with the fall in periodate concentration. It seemed possible that the reaction might be affected by the surface of the vessel; but the time course of the reaction was unaltered either in a flask lined with paraffin wax or when fine glass particles ("Ballotini" No. 12) were added. Possibly, acceleration of periodate consumption is due to increasing numbers of points of attack from the disruption of the molecule; but the second stage with 3 : 4-dimethyl and 3 : 4 : 6-trimethyl glucose (see above) does not show acceleration (Expt. 13).

Bell *et al.* (*loc. cit.*) suggested that the chemical nature of the buffer can influence the course of reactions with neutral periodate. But when 2 : 3 : 6-trimethyl, 2 : 4 : 6-trimethyl, and 2 : 3 : 4 : 6-tetramethyl glucose are treated with periodate brought initially to pH 7·6 with sodium hydroxide, with no extra buffer, the rate with each sugar is about the same, during the first 100—150 hours, as in presence of phosphate, but then falls with increasing acidity (Fig. 3). With 2 : 3 : 4-trimethyl glucose the initial rate is even greater than in phosphate (Fig. 1). The pH changes with the 2 : 3 : 6-trimethyl sugar again suggest no preferential attack at $C_{(4)}$ and $C_{(5)}$ (Expt. 19).

Type (iii) reactions also proceeded, but very slowly, at pH 5; compounds which reacted with neutral periodate all underwent some reaction with metaperiodate, some even showing typical acceleration (Expt. 7). Of compounds not reacting at pH 7·5, those tested were also unattacked at pH 5. It may be that $H_3IO_6^{--}$ is more effective for Type (iii) reactions than $H_4IO_6^-$, since the former is absent from metaperiodate solutions.

Experimental

M. p.s (uncorr.) and rotations (measured in 2-dm. tubes) were determined on specimens dried over phosphoric oxide *in vacuo* at room temperature. Evaporations were done under reduced pressure, and solvents distilled in glass were used for recrystallisations. Paper chromatograms, 2% sugar solutions being used, were run with *n*-butanol–water on Whatman No. 1 papers at room temperature and sprayed with aniline hydrogen phthalate. pH was measured by the glass electrode.

2 : 3 : 4-*Trimethyl Glucose*.—2 : 3 : 4-Trimethyl 1 : 6-anhydro-β-glucose, purified to constant m. p. (see table below), was hydrolysed (5% solution in N-hydrochloric acid) at 95—100° to constant rotation (8 hours). After isolation (silver carbonate method) the sugar, dried at 0·05 mm. for 8 hours, had $[\alpha]_D^{20}$ +70·4° in water at equilibrium. From the constancy of the rotation, such drying did not cause anhydride formation. The latter occurs (Irvine and Oldham, *J.*, 1921, **119**, 1744) during the usual purification by distillation, so partition chromatography (Bell, *J.*, 1944, 473; Bell *et al.*, *loc. cit.*) was used. Anhydro-compound (about 9%) was removed by elution with chloroform (7 column-lengths). The sugar was eluted with *n*-butanol–chloroform and, after removal of solvents, dissolved in ether, filtered, evaporated, and dried as before. The syrup (about 83%) had $[\alpha]_D^{20}$ +78·7° in water (*c*, 2·5) at equilibrium, n_D^{20} 1·4700 (decrement for rise of 1°, 0·00035 from 20° to 25°). This rotation is more than 10° higher than any previously recorded (for references, see Bourne and Peat, *Adv. Carbohydrate Chem.*, 1950, **5**, 145). Reduction of hypoiodite was determined under Macleod and Robison's conditions (*Biochem. J.*, 1929, **23**, 517) but on a larger scale (14 mg. of sugar); complete in 30 minutes, it was 100·0% of the theoretical. As in addition the product gave a single compact spot on paper chromatograms, its $[\alpha]_D$ is probably near that of the pure sugar.

Other Compounds.—All sugars gave single spots on paper chromatograms. A hydrolysate of the tetramethyl glucoside contained trimethyl sugar (considerably less than 1%, by paper chromatography); this possibly arose during hydrolysis. Characteristics were (G = glucose; M = β-methylglucoside; eqm. = equilibrium):

Compound	M. p.	$[\alpha]_D$ (water)
2 : 3 : 6-Trimethyl G	109—113°	+68·9° (18°, eqm.)
2 : 4 : 6-Trimethyl G	118—120	+77·0° (16°, eqm.)
2 : 3 : 4 : 6-Tetramethyl G	90—92	+81·5° (19°, eqm.) [a]
2 : 3 : 4 : 6-Tetramethyl M	36—37	−18·2° (19°) [b]
1 : 6-Anhydro-glucopyranose	181—182	−66·9° (18°)
2 : 3 : 4-Trimethyl 1 : 6-anhydro-β-G	59—60 [c]	−62·3° (18°)
2-Methoxyethanol [d]	124·0—124·3 (b. p.)	—
n-Butyl methyl ether [d]	68—69 (b. p.)	—

For 3 : 4-dimethylglucose and β-methylglucoside, see Bell and Greville (*loc. cit.*). For 3 : 4 : 6-trimethyl glucose, its β-methylglucoside, and 2-benzoyl 3 : 4 : 6-trimethyl β-methylglucoside, see Greville and Northcote (*J.*, 1952, 1957).

[a] Fits West and Holden's equation (*Org. Synth.*, 1940, **20**, 97). [b] n_D^{23} 1·4394 (decrement for rise of 1°, 0·00040 from 23° to 33°). [c] Note difference from literature values. [d] Peroxide-free.

Reactions with Periodate.—Procedures. Reactions were carried out in glass-stoppered volumetric flasks in the dark, and, unless otherwise stated, in a thermostat at 22°. Simultaneous control determinations on the reagents were always carried out. Glass-distilled water and "AnalaR" reagents were used. The crystalline $NaIO_4$ contained no free acid (for test, see Halsall *et al.*, *loc. cit.*). Unless otherwise stated, sugars were dissolved in water immediately before the reaction mixture was set up. Reactions were carried out (*a*) with metaperiodate (0·02M, pH 5·1); (*b*) with periodate at pH 7·5 in phosphate buffer (0·025M-sodium phosphate pH 7·5, 0·01M-$NaIO_4$, and 0·003N-sodium hydroxide); and (*c*) with periodate, initially pH 7·6, without addition of buffer, the solution containing 0·01M-$NaIO_4$ with the requisite sodium hydroxide (0·305 ml. of 0·1N per ml. of 0·1M-$NaIO_4$ gave pH 7·65). Precipitation never occurred with solutions (*b*) and (*c*) as here, but with (*b*) a precipitate appeared after a few days if all concentrations were doubled.

Consumption of periodate was measured by titration of 1- or 2-ml. samples with 0·005M-arsenite after addition of 4 ml. of 0·067M-phosphate of pH 7·5 and excess of potassium iodide. Polyvinyl alcohol containing 20 mol. % of residual acetyl (Miller and Bracken, *J.*, 1951, 1933) as indicator permitted titration to less than 0·005 ml. Volatile acid was determined as previously (Bell and Greville, *loc. cit.*). Formic acid was identified (1) by redistillation with mercuric sulphate (Bell and Greville, *loc. cit.*), (2) by testing evaporated neutralised distillate with chromotropic acid, before and after reduction with magnesium (Grant, *Analyt. Chem.*, 1948, **20**, 267), colours being compared by eye with standards.

Periodate consumed and acid formed are, unless otherwise indicated, expressed as moles (or equivs.) per mole of sugar initially present.

(*a*) *Reactions with metaperiodate.* (1) 2 : 3 : 6-Trimethyl glucose (9·5 mM), 2 : 4 : 6-trimethyl glucose (9·5 mM), and 2 : 3 : 4-trimethyl glucose (9·0 mM) were treated with 2·1 moles of metaperiodate :

Reaction time (hours)	8	12	25	50	100	200	480
Periodate consumed :							
2 : 3 : 6-Compound	0·00	—	0·01	0·01	0·03	0·06	—
2 : 4 : 6-Compound	0·00	—	0·00	0·01	0·02	0·04	—
2 : 3 : 4-Compound	0·02	0·06	0·15	0·27	0·46	0·78	1·25

2 : 3 : 4-Trimethyl glucose (11·1 mM) was also treated with 2·02 moles of metaperiodate for 12 hours. Periodate consumed : 0·10. Volatile acid formed : 0·00.

(2) (i) 3 : 4 : 6-Trimethyl glucose (*A*) and 3 : 4-dimethyl glucose (*B*) (each 9·0 mM), were treated with 2·13 moles of metaperiodate :

Reaction time (minutes)	5·7	10·5	20·7	42	63	85	135	480
Periodate consumed : (*A*)	0·27	0·32	0·40	—	0·69	—	0·91	1·00
(*B*)	0·59	0·62	0·67	0·76	—	0·88	—	1·00

(ii) 3 : 4 : 6-Trimethyl glucose (9·8 mM) was treated with 2·11 moles of metaperiodate at *ca.* 18°. Periodate consumed : 0·90 (3·2 hours), 0·99 (7·75 h.), 1·00 (24, 46, 70 h.), 1·01 (94 h.).

(iii) 3 : 4-Dimethyl glucose (9·2 mM) was treated with 2·08 moles of metaperiodate. Periodate consumed : 0·90 (1·5 hours), 0·99 (4 h.), 1·01 (7 and 53 h.), 1·04 (102 h.).

(3) 3 : 4 : 6-Trimethyl glucose (17·4 mM) was treated with 1·50 moles of metaperiodate :

Reaction time (hours)	0·58	20	45
Periodate consumed	0·65	1·00	1·01
Volatile acid formed	0·64	0·97	0·99

Redistillation with mercuric sulphate eliminated the volatile acid. The chromotropic test after reduction with magnesium gave about the expected intensity of colour; no formaldehyde was present before reduction and no formic acid in the control.

(4) To demonstrate the determination of 3 : 4 : 6-trimethyl glucose in the presence of the other trimethyl glucopyranoses, reaction mixtures (10 ml., containing 216 μmol. of metaperiodate) were set up as shown :

	Periodate consumed (μmols.)	Volatile acid formed (μequivs.)
(i) 101 μmol. 2 : 3 : 4-compound + 99 μmol. 2 : 3 : 6-compound + 105 μmol. 2 : 4 : 6-compound (12 hours)	10	0
(ii) As (i), + 101 μmol. 3 : 4 : 6-compound	108	102
(iii) Diff. due to 101 μmol. 3 : 4 : 6-compound	98	102
(iv) As (i), 60 hours	—	2

(5) 3 : 4-Dimethyl glucose (9·8 mM) was treated with 2·03 moles of metaperiodate for 12 hours. Periodate consumed, 1·00; volatile acid formed, 1·02.

(6) 2 : 3 : 4 : 6-Tetramethyl glucose (10·1 mM) was treated with 2·1 moles of metaperiodate. Periodate consumed : 0·00 (23, 51, 75 hours), 0·04 (141 h.), 0·12 (210 h.), 0·18 (289 h.), 0·28 (339 h.).

(7) 2 : 3 : 4 : 6-Tetramethyl β-methylglucoside (9·2 mM) was treated with 2·11 moles of metaperiodate. Periodate consumed : 0·00 (23 hours), 0·04 (142 h.), 0·13 (235 h.), 0·18 (281 h.), 0·26 (330 h.).

(8) 1 : 6-Anhydro-β-glucopyranose (9·0 mM) was treated with 3·01 moles of metaperiodate. Periodate consumed : 0·92 (1·13 hours), 1·43 (2·84 h.), 1·82 (6·67 h.), 2·01 (24, 53 h.). Acid present after 24 hours (by titration with sodium hydroxide after addition of excess of ethylene glycol, with methyl-red) : 1·00 equiv. per mole.

(9) 2-Methoxyethanol and *n*-butyl methyl ether (both 9·3 mM) were treated with 2·1 moles of metaperiodate. Periodate consumed: 0·00 (369 and 309 hours, respectively).

(*b*) *Reactions with periodate in phosphate*, pH 7·5. (10) 2 : 3 : 6-Trimethyl glucose (4·7 mM) was treated with 2·11 moles of periodate (Fig. 2), the sugar being in 2% solution in water for 40 hours before the reaction mixture was set up. An identical curve was obtained when the sugar was dissolved immediately before the start of the reaction. The compound (2·45 mM) was also treated with 4·06 moles of periodate. Periodate consumed: 0·56 (135 hours), 1·53 (267 h.), 2·96 (437 h.).

(11) 2 : 4 : 6-Trimethyl glucose (5·2 mM) was treated with 2·09 moles of periodate (Fig. 2). The sugar (2·35 mM) was also treated with 4·13 moles; periodate consumed: 0·25 (94 hours), 2·44 (219 h.), 4·13 (294 h.). As in (10), previous mutarotation had no effect on the shape of the curve.

(12) 2 : 3 : 4-Trimethyl glucose (4·7 mM) was treated with 2·08 moles of periodate (Fig. 1).

(13) (i) 3 : 4 : 6-Trimethyl glucose (9·0 mM) was treated with 2·11 moles of periodate at *ca.* 18° (cf. Expt. 2, ii). Periodate consumed: 1·04 (2·5 hours), 1·14 (9 h.), 1·24 (25 h.), 1·39 (47 h.), 1·55 (72 h.), 1·88 (125 h.).

(ii) 3 : 4 : 6-Trimethyl glucose (1·9 mM) was treated with 5·02 moles of periodate. Periodate consumed: 4·42 (336 hours).

(iii) 3 : 4-Dimethyl glucose (4·6 mM) was treated with 2·08 moles of periodate (cf. Expt. 2, iii). Periodate consumed: 0·91 (0·6 hour), 1·10 (7 h.), 1·45 (26 h.), 1·86 (55 h.), 2·03 (77 h.), 2·08 (102 h.).

(14) (i) 2 : 3 : 4 : 6-Tetramethyl glucose (5·2 mM) was treated with 2·09 moles of periodate. Periodate consumed: 0·04 (23 hours), 0·16 (47 h.), 0·36 (72 h.), 0·68 (99 h.), 1·02 (117 h.), 1·40 (135 h.), 1·83 (159 h.), 2·09 (192 h.). As in (10) previous mutarotation had a negligible effect on the shape of the curve.

(ii) The sugar (1·55 mM) was treated with 6·06 moles of periodate. Periodate consumed: 1·05 (99 hours), 6·06 (235 h.).

(iii) The sugar (0·40 mM) was treated with 24·2 moles of periodate. Periodate consumed: 1·0 (77 hours), 6·9 (125 h.), 10·8 (168 h.), 12·2 (215 h.), 13·6 (356 h.), 14·4 (478 h.), 14·5 (545, 601, 669 h.).

(iv) Volatile acid production and corresponding periodate consumption are shown:

Expt.	Sugar (mM)	Initial periodate	Periodate consumed	Volatile acid
(A)	1·6	6	2·7	0·9
(B)	1·6	6	6·0	1·2
(C)	0·4	24	14·6	0·3

With (B), redistillation with mercuric sulphate eliminated the volatile acid, and the chromotropic acid test gave the expected intensity of colour.

(15) (i) 3 : 4-Dimethyl β-methylglucoside (4·65 mM) was treated with 2·09 moles, 3 : 4 : 6-trimethyl β-methylglucoside (4·15 mM) with 2·33 moles, and 2 : 3 : 4 : 6-tetramethyl β-methylglucoside (4·6 mM) with 2·09 moles of periodate:

Time (hours)	50	100	150	200	250	300
Me_2	0·08	0·29	0·71	1·30	1·90	2·09
Me_3	0·12	0·62	1·40	2·01	2·33	—
Me_4	0·33	1·16	1·95	2·09	—	—

(ii) In addition, the tetramethyl glucoside (0·52 mM) was treated with 18·5 moles of periodate. Periodate consumed: 0·3 (30 hours), 4·7 (103 h.), 8·3 (168 h.), 12·2 (293 h.), 14·5 (500 h.), 15·1 (600 h.).

(iii) The tetramethyl glucoside (0·42 mM) was treated with 23·9 moles of periodate for 530 hours. Periodate consumed, 15·8; volatile acid produced, 0·3.

(16) The substances below did not consume any periodate:

Compound	Concn. (mM)	Periodate (moles)	Reaction time (hours)
2 : 3 : 4-Trimethyl 1 : 6-anhydro-β-glucose	5·0	2·1	291
2-Benzoyl 3 : 4 : 6-trimethyl β-methylglucoside	3·2	3·1	258
	1·3	7·7	258
2-Methoxyethanol	4·6	2·1	336
	1·5	6·3	213
n-Butyl methyl ether	4·6	2·1	309
	1·5	6·3	309

(17) Formic acid (" AnalaR "; 5 mM) was treated with 2·07 moles of periodate. Periodate consumed: 0·035 (29 hours), 0·05 (48 h.), 0·06 (208 h), 0·065 (308 h.).

(*c*) *Reactions with periodate* pH 7·6 *without addition of buffer.* (18) 2 : 3 : 4-Trimethyl glucose (5·6 mM) was treated with 2·08 moles of periodate (Fig. 1). pH values: initial, 7·63; final, 5·15.

(19) 2 : 3 : 6-Trimethyl glucose (4·65 mM) was treated with 2·09 moles of periodate and 2 : 4 : 6-trimethyl glucose (4·6 mM) with 2·13 moles (Fig. 3). pH values (16°) were measured at intervals. The control remained throughout at pH 7·64—7·66.

Periodate consumed	0·71	0·73	0·95	1·01	1·13	1·16	1·45
pH : 2 : 3 : 6-compound	—	7·06	6·86	—	6·58	—	—
2 : 4 : 6-compound	6·96	—	—	6·47	—	6·03	4·92

(20) 2 : 3 : 4 : 6-Tetramethyl glucose (4·55 mM) was treated with 2·10 moles of periodate (Fig. 3). Initial pH: 7·64.

We have pleasure in thanking Dr. D. J. Bell for the interest he has taken in this work and for helpful advice. Polyvinyl alcohol indicator was kindly given by the Research and Development Department of the British Oxygen Company Ltd.

BIOCHEMICAL LABORATORY,
TENNIS COURT ROAD, CAMBRIDGE. [*Received, December 20th,* 1951.]

NOTES.

361. 4 : 5- *and* 3 : 6-*Dinitronaphthalic Anhydrides.*

By F. BELL.

4 : 5-DINITRONAPHTHALIC ANHYDRIDE has been prepared by (*a*) oxidation of dinitroacenaphthene (Mayer and Kaufmann, *Ber.*, 1920, **53**, 296), (*b*) oxidation of dinitroacenaphthenequinone (Rowe and Davies, *J.*, 1920, **117**, 1344), and (*c*) nitration of 4-nitronaphthalic anhydride (Rule and Thompson, *J.*, 1937, 1766). It was oriented by Rule and Brown (*J.*, 1934, 171). Rule and Thompson (*loc. cit.*) showed that the m. p. of the anhydride could be raised to 327—329° by repeated crystallisation from nitric acid and that it was best characterised by interaction with *o*-phenylenediamine to give a benziminazole derivative, m. p. 370°. 4 : 5-Dinitronaphthalic acid does not appear to have been described. If hydrochloric acid is added to a solution of the anhydride in aqueous sodium carbonate the resulting precipitate, which after drying darkens at 260° and melts indefinitely, is insoluble in boiling water and yields the anhydride when crystallised from other solvents.

The nitration of naphthalic anhydride was described by Anselm and Zuckmayer (*Ber.*, 1899, **32**, 3284) and, independently, by Francesconi and Bargellini (*Gazzetta*, 1902, (2), **32**, 94). The former authors by crystallisation of the nitration product from benzene obtained yellow-brown needles, m. p. 214°, of the dinitro-anhydride whereas the latter authors crystallised the product from water and obtained a dinitro-acid in silvery-white leaflets, m. p. 208—210°. Francesconi and Bargellini record that the acid dissolves in concentrated nitric acid to give a small yield of a compound, m. p. 266°, which was not analysed or examined further. Mihailescu and Steopoe (*Bull. Sect. Scient. Acad. Roumaine*, 1923, **8**, 102) describe the conversion of naphthalic anhydride into dinitronaphthalic anhydride, m. p. 207—208°, but state that their compound is much more soluble than would be gathered from Anselm and Zuckmayer's description. Rule and Brown (*loc. cit.*) first established that the acid was 3 : 6-dinitronaphthalic acid by decarboxylation to 2 : 7-dinitronaphthalene. Rule and Thompson (*loc. cit.*) state that the dinitro-acid can be

recrystallised unchanged from boiling nitrobenzene but is converted into the anhydride, m. p. 330°, by recrystallisation from boiling nitric acid. Francesconi and Bargellini's compound, m. p. 266°, is regarded by them as the impure anhydride. The 3 : 6-dinitro-acid was characterised by reaction with *o*-phenylenediamine to give a benziminazole derivative, m. p. 301°.

Hodgson and Ward (*J.*, 1945, 590) by the method of Anselm and Zuckmayer obtained an 85% yield of the crude 3 : 6-dinitro-anhydride, which was practically insoluble in water but formed needles, m. p. 214°, from toluene or xylene. Solution of the dinitro-anhydride (10 g.) in boiling nitric acid furnished tetranitronaphthalene (0·2 g.), m. p. >295° (decomp.), soluble in 10% sodium carbonate solution and reprecipitated as a colourless solid, m. p. >310° (decomp.). Francesconi and Bargellini's compound, m. p. 266°, is taken by these authors to be impure tetranitronaphthalene.

It will be seen that the various descriptions of the nitration of naphthalic anhydride do not accord and, further, it is difficult to reconcile the exclusive nitration of naphthalic anhydride in the 3 : 6-positions with the nitration of 4-nitronaphthalic anhydride, under very similar conditions, to the 4 : 5-dinitro-derivative only. The experiments were repeated in the hope of resolving these anomalies.

Experimental.—4 : 5-Dinitronaphthalic anhydride was prepared by methods (*a*), (*b*) [dinitro-acenaphthenequinone has m. p. 317° (lit., >300°)], and (*c*). Rule and Thompson's method gave the yield stated (37%); slight modification results in improvement. A mixture of nitric acid (*d* 1·5; 2 c.c.) and sulphuric acid (3 c.c.) was added to 4-nitronaphthalic anhydride (3 g.) in sulphuric acid (18 c.c.). The resultant solution was placed on a boiling water-bath for ½ hour, cooled, and poured on ice. The precipitate (2·85 g.) was crystallised from boiling nitric acid giving 1·9 g. (54%), m. p. 321°. The nitric acid mother-liquor on dilution with water remained clear.

Nitration of Naphthalic Anhydride.—Hodgson and Ward's method gave the stated yield of crude product. Solution of the crude product (22 g.) in hot concentrated nitric acid gave on cooling 4 : 5-dinitronaphthalic anhydride (1·6 g.), m. p. 322°, alone or mixed with an authentic specimen and unchanged by recrystallisation from acetic anhydride. Identity was further confirmed by interaction with *o*-phenylenediamine. The nitric acid filtrate, when poured into water, gave 3 : 6-dinitronaphthalic anhydride (18 g.), m. p. 216° after crystallisation from xylene or acetic anhdride. The anhydride can be recrystallised from nitric acid (about 4 c.c. for 1 g.) and then separates in stout prisms. The pure anhydride can be heated with concentrated nitric acid for a considerable time without change. Solution of the anhydride in aqueous sodium carbonate followed by reprecipitation with hydrochloric acid furnishes 3 : 6-dinitronaphthalic acid, which crystallises from boiling water in silvery scales, m. p. 212°. It is insoluble in boiling xylene but dissolves in boiling acetic anhydride with some decomposition leading to evolution of oxides of nitrogen.

It appears probable, therefore, that Francesconi and Bargellini's compound, m. p. 266°, Rule and Thompson's 3 : 6-dinitronaphthalic anhydride, and Hodgson and Ward's tetranitronaphthalene were all 4 : 5-dinitronaphthalic anhydride in varying degrees of purity. Further, Rule and Thompson in preparing the benziminazole, m. p. 301°, must have used the " acid " and not the " anhydride, m. p. 330° " or they would have perceived that the latter was actually the 4 : 5-dinitro-compound.

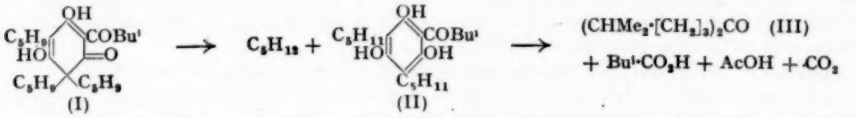
Since naphthalic anhydride on nitration gives some 4 : 5-dinitro-derivative and since 4-nitronaphthalic anhydride gives a yield of only 54% of the 4 : 5-dinitro-derivative (leaving it possible that the loss is in part occasioned by the production of the 4 : 6-dinitro-derivative), the nitration results can be regarded as reconciled.

HERIOT-WATT COLLEGE, EDINBURGH. [*Received, February 18th,* 1952.]

362. *Structure of the Hydrogenation Product of Lupulone.*

By M. Verzele.

Lupulone (I), one of the bitter constituents of hops, is cleaved on hydrogenation to 2-methylbutane and a product believed to be (II) (Wöllmer, *Ber.*, 1925, **58**, 672) which on degradation by concentrated alkali affords an oily ketone believed to be 2 : 10-dimethylundecan-6-one (III), as well as *iso*valeric and acetic acids and carbon dioxide (cf. Verzele and Govaert, *Bull. Soc. chim. Belg.*, 1949, **58**, 432, for a similar reaction with lupulone).



The structure of (III), and hence of (II) and (I), has been confirmed by synthesis from 5-methylhexanoic acid by passage over thoria.

Experimental.—The hydrogenation product (5·25 g.; obtained from 6·25 g. of lupulone by Wöllmer's method, *loc. cit.*) gave, by alkali fission (see Verzele *et al.*, *loc. cit.*), *iso*valeric acid (1·25 g., 75%), b. p. 174—175° (amide, m. p. 128° alone or mixed with authentic material), and 2 : 10-dimethylundecan-6-one (2·25 g., 75%), b. p. 135—137°/20 mm., m. p. −30°. The *semicarbazone* of the ketone, prepared in the usual way, had m. p. 83° (Found : N, 16·4, 16·3. $C_{14}H_{29}ON_3$ requires N, 16·7%).

Passage of 5-methylhexanoic acid (13 g.) over thoria at 420° gave sweet-smelling 2 : 10-dimethylundecan-6-one (8 g., 73%), b. p. 127°/13 mm., the semicarbazone of which had m. p. 82° alone or mixed with the material mentioned above.

Laboratorium voor Organische Chemie,
Plateaustraat 22, Ghent, Belgium.

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363. *Preparation of 3-Aryl-7-hydroxy-4-methylcoumarins.*

By Walter Freund.

Meerwein, Buchner, and van Emster (*J. pr. Chem.*, 1939, **152**, 237; B.P. 480 617) have arylated coumarin and 7-hydroxycoumarin (umbelliferone) at position 3 by treating these compounds with diazo-solutions in aqueous acetone, the reaction mixture being buffered with sodium acetate and chloroacetate respectively. 4-Methylumbelliferone gives very poor yields, but l'Ecuyer and Olivier (*Canad. J. Res.*, 1950, **28**, *B*, 648) obtained the corresponding stilbenes in good yield from β-methylcinnamic acid and diazo-compounds under Meerwein's conditions. 7-Hydroxy-3-*p*-methoxyphenyl-4-methylcoumarin has been prepared by another method by Mentzer, Gley, Molho, and Billet (*Bull. Soc. chim.*, 1946, 271); it is weakly œstrogenic (Gley and Mentzer, *Compt. rend. Soc. Biol.*, 1945, 139, 1055).

Experimental.—(M. p.s are uncorrected.)

A filtered diazo-solution prepared from *p*-chloroaniline (6·4 g.), sodium nitrite (3·65 g.), and 25% hydrochloric acid (22 g.) was added to a mixture of 4-methylumbelliferone (8·8 g.) in acetone (800 c.c.), and sodium chloroacetate (25 g.) in a small amount of water, the pH being then approx. 5. No gas evolution was noticeable (temp. 20°). On gentle warming and addition of copper chloride (3 g.) in a small amount of water, gas evolution set in. Finally, the solution was heated to 35° with continual shaking. The mixture was steam-distilled to remove the acetone. The remaining solid was extracted several times with boiling water, and the residue digested with a little cold alcohol and dried on a porous tile. On recrystallisation from glacial acetic acid, a small amount of 3-p-*chlorophenyl-7-hydroxy-4-methylcoumarin* separated in plates, m. p. 233—234° (Found : C, 67·0, 67·1; H, 4·0, 4·0; Cl, 12·4. $C_{16}H_{11}O_3Cl$ requires C, 67·0; H, 3·8; Cl, 12·4%).

3-p-*Bromophenyl*-7-*hydroxy*-4-*methylcoumarin*, prepared similarly, separated from glacial acetic acid in plates, m. p. 256—259° (Found: C, 58·3, 58·1; H, 3·5, 3·4; Br, 24·3. $C_{16}H_{11}O_3Br$ requires C, 58·0; H, 3·3; Br, 24·2%).

7-Hydroxy-3-*p*-methoxyphenyl-4-methylcoumarin was also prepared similarly, except that 850 c.c. of acetone were used. The yield was very poor. The m. p. was 230—231° (Mentzer *et al.*, *loc. cit.*, give m. p. 232°) (Found: C, 72·4, 72·4; H, 5·0, 5·1; MeO, 11·1. Calc. for $C_{17}H_{14}O_4$: C, 72·3; H, 5·0; MeO, 11·0%).

I thank Dr. K. F. Tettweiler, formerly of the University of Melbourne, for the microanalyses. This work was supported in part by a grant from the National Council for Health and Medical Research, Canberra.

PHYSIOLOGY DEPARTMENT, THE UNIVERSITY, MELBOURNE. [*Received, November 12th*, 1951.]

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364. *Adsorption from Binary Solutions of Completely Miscible Liquids. Part II.* Thermodynamic Requirement for Complete Preferential Adsorption.*

By G. A. H. ELTON.

THE various types of isotherms obtained experimentally for adsorption from a binary solution of two completely miscible liquids A and B were discussed in Part I,* where it was shown that, from measurements of concentration change brought about by adsorption, the mole-fraction of each component in the adsorbed surface layer could be calculated by using the expressions

$$x_B^s = \frac{A(x_B + \Delta x_B) - a_A(n_A + n_B)\Delta x_B}{A + (n_A + n_B)(a_B - a_A)\Delta x_B} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$x_A^s = 1 - x_B^s \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where x_A^s, x_B^s are the surface mole-fractions of A and B respectively, x_B the equilibrium bulk mole-fraction of B, Δx_B the change in bulk mole-fraction produced by adsorption, a_A, a_B the effective areas per mole in the surface layer, n_A, n_B the number of moles of each component in the whole system, and A the surface area of the adsorbent. If the surface mole-fraction of one component is found to exceed its bulk mole-fraction over the whole range between zero and unity, we may say that it is "completely preferred" by the adsorbent. Failing this, the graph of x_B^s against x_B will cut the line $x_B^s = x_B$ at some point intermediate between zero and unity: *i.e.*, the "net adsorption" of B changes sign at this point.

It is of interest to examine the thermodynamic requirements for the existence of each of these cases. For equilibrium between the adsorbed layer and solution in a given solid–solution system, we have the following general relations between the activities a_A, a_B, in the solution, and a_A^s, a_B^s in the adsorbed layer:

$$a_A^s/a_A = \exp\{[(\mu_A)_0 - (\mu_A^s)_0]/RT\} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$a_B^s/a_B = \exp\{[(\mu_B)_0 - (\mu_B^s)_0]/RT\} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $(\mu_A)_0$, $(\mu_B)_0$ are the chemical potentials of A and B in arbitrarily defined standard states in the solution, and $(\mu_A^s)_0$, $(\mu_B^s)_0$ are the corresponding chemical potentials in suitable standard states in the surface layer. Convenient standard states which we will take are (i) for $(\mu_A)_0$ and $(\mu_B)_0$, infinite dilution for the appropriate component in the bulk solution, and (ii) for $(\mu_A^s)_0$ and $(\mu_B^s)_0$, infinite dilution for the appropriate component in the surface layer. The quantities $[(\mu_A)_0 - (\mu_A^s)_0]$ and $[(\mu_B)_0 - (\mu_B^s)_0]$ may be conveniently termed the "adsorption potentials" of A and B. By analogy with the work of Fu, Hansen, and Bartell (*J. Physical Chem.*, 1948, **52**, 374) we may write, in the limit as x_A tends to zero, $(x_A^s/x_A)_0 = (a_A^s/a_A)_0$, and as x_B tends to zero, $(x_B^s/x_B)_0 = (a_B^s/a_B)_0$. For complete preferential adsorption of one component, the adsorption potentials must, in order to

* Part I, *J.*, 1951, 2958.

produce a graph of x_B' against x_B of the appropriate shape, be opposite in sign, whilst in all other cases they will be of similar sign. Inserting these requirements in equations (3) and (4), we reach the conclusion that if both components have positive adsorption potentials, no preferential adsorption can occur. Since, from kinetic considerations, negative values of the adsorption potential are not very likely, it is to be expected that cases of complete preferential adsorption will be rarely found. This seems in practice to be the case (see, *e.g.*, Bartell and Sloan, *J. Amer. Chem. Soc.*, 1929, **51**, 1643).

From the example of the calculation of a surface mole-fraction isotherm by use of equation (1), given in Part I (*loc. cit.*), we may obtain approximate values of the adsorption potentials of the two components on charcoal from the limiting slopes of the surface mole-fraction isotherms. The values obtained are 1·0 kcal. for methanol, and 1·1 kcal. for carbon tetrachloride.

BATTERSEA POLYTECHNIC, S.W.11. [*Received, January 14th*, 1952.]

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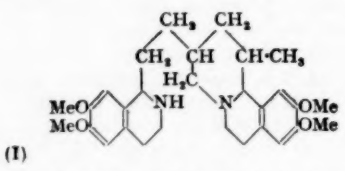
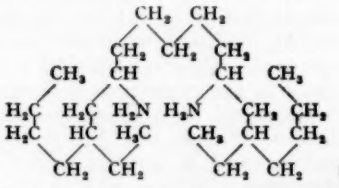
365. *Structure and Amœbicidal Activity. Part III.* Aliphatic Diamines.*

By D. MURIEL HALL, SARDAR MAHBOOB, and E. E. TURNER.

SINCE there is little prospect of our being able to continue the synthetic work described in Parts I and II of this series (*J.*, 1950, 1842; 1952, 149) we should like to draw attention to the curious fact that 7 : 13-diamino-5 : 15-diethylnonadecane (II) which we synthesised under the stimulus of Pyman's formula (I) for emetine (*J.*, 1927, 1069) [subsequently shown to be incorrect (Robinson, *Nature*, 1948, **162**, 524; Pailer and Porschinski, *Monatsh.*, 1949, **80**, 94; Battersby, Openshaw, and Wood, *Experientia*, 1949, **5**, 114; Battersby and Openshaw, *J.*, 1949, 3207)], in a particular configuration bears a pictorial resemblance to (I). As stated in Part II, this base (II) has as high an amœbicidal activity *in vitro* as emetine itself.



(I)



(II)

A further remarkable result is that within the series $NH_2{\cdot}CHR{\cdot}[CH_2]_n{\cdot}CHR{\cdot}NH_2,2HCl$, R being 2-ethylhexyl, the amœbicidal activity is 1 in 100,000 for $n = 3$, is zero for $n = 4$, but reappears augmented for $n = 5$. (The first two compounds are described in Part I and the third in Part II.)

We now describe the synthesis of 5 : 9-diamino-7 : 7-dimethyltridecane dihydrochloride, the preparation of which was complicated by the presence of a *neo*pentyl structure and by the fact that the final dihydrochloride was more than usually deliquescent. This hydrochloride has an activity *in vitro* of 1 in 1000 against *Entamœba histolytica*.

Experimental.—Microanalyses by Drs. Weiler and Strauss.

7 : 7-*Dimethyltridecane*-5 : 5 : 9 : 9-*tetracarboxylic acid*. Condensation of 1 : 3-dibromo-2 : 2-dimethylpropane with an alcoholic solution of sodium ethoxide and ethyl *n*-butylmalonate during 136 hours gave ethyl 7 : 7-dimethyltridecane-5 : 5 : 9 : 9-tetracarboxylate (13%), b. p. 164°/4 mm. The *acid* derived from this crude ester crystallised, with partial decarboxylation, from benzene–light petroleum (b. p. 60—80°) and had m. p. 155—157° (Found : C, 60·8; H, 9·5. $C_{19}H_{32}O_8$ requires C, 58·7; H, 8·3%).

5 : 9-*Diamino*-7 : 7-*dimethyltridecane*. 7 : 7-Dimethyltridecane-5 : 9-dicarboxylic acid (5·8 g.), obtained as a thick liquid by heating the tetracarboxylic acid at 210°, was dissolved in benzene

* Part II, *J.*, 1952, 149.

(50 c.c.), and concentrated sulphuric acid (30 c.c.) was added. Sodium azide (2·6 g.) was added and the temperature kept at 40—45° until reaction was complete. The mixture was cooled, diluted with ice, and made alkaline with 30% sodium hydroxide at <30°. The base was extracted with benzene–ether. Part of it was converted into the *dihydrochloride* by passing in hydrogen chloride and removing the solvent in a vacuum. It was exceedingly deliquescent and decomposed >100° (Found: C, 58·2; H, 11·7; N, 8·55; Cl, 21·3. $C_{15}H_{36}N_2Cl_2$ requires C, 57·1; H, 11·5; N, 8·85; Cl, 22·5%).

We thank Dr. J. D. Fulton of the National Institute for Medical Research for the biological tests, and the Medical Research Council and Imperial Chemical Industries Limited for financial assistance.

BEDFORD COLLEGE, UNIVERSITY OF LONDON. [*Received, January 19th*, 1952.]

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366. *A Synthesis of* 3 : 4 : 6-*Trimethyl Glucose.*

By G. D. GREVILLE and D. H. NORTHCOTE.

3 : 4 : 6-TRIMETHYL GLUCOSE has been obtained during structural investigation of certain polysaccharides (Granichstädten and Percival, *J.*, 1943, **54**; Putman, Potter, Hodgson, and Hassid, *J. Amer. Chem. Soc.*, 1950, **72**, 5024), and its β-methylglucoside has been prepared from 4 : 6-dimethyl 2 : 3-anhydro-β-methylalloside (Peat and Wiggins, *J.*, 1938, 1810). Haworth, Hirst, and Panizzon (*J.*, 1934, 154) synthesised the sugar in an amorphous state by a route through 2-tosyl β-methylglucoside. Sundberg, McCloskey, Rees, and Coleman (*J. Amer. Chem. Soc.*, 1945, **67**, 1080) obtained it in crystalline form from 2-benzyl 3-methyl β-methylglucoside. In this laboratory we had easy access to 2-benzoyl 3-methyl β-methylglucoside (Bell and Greville, *J.*, 1950, 1902), and Dr. D. J. Bell suggested that, provided the benzoyl radical did not migrate, a simple synthesis of the sugar should be possible from this substance. We therefore methylated it to obtain 2-benzoyl 3 : 4 : 6-trimethyl β-methylglucoside which, when heated under reflux with aqueous ethanolic sodium hydroxide, was converted easily and in good yield into crystalline 3 : 4 : 6-trimethyl β-methylglucoside. The latter was then hydrolysed to the crystalline sugar.

Experimental.—M. p.s (uncorr.) and rotations (measured in 2-dm. tubes) were determined on specimens dried *in vacuo* over phosphoric oxide at room temperature. Elementary analyses were by Drs. Weiler and Strauss, Oxford. Solvents were removed under reduced pressure, and solvents distilled in glass were used for recrystallisations.

2-Benzoyl 3 : 4 : 6-*trimethyl* β-*methylglucoside.* 2-Benzoyl 3-methyl β-methylglucoside (Dewar and Fort, *J.*, 1944, 496; prepared according to Bell and Greville, *loc. cit.*) (1·42 g.) was methylated three times with Purdie's reagents, *ca.* 20 mols. of methyl iodide being used each time. The product (1·46 g.) crystallised on seeding, and recrystallisation from light petroleum (b. p. 60—80°) gave *2-benzoyl* 3 : 4 : 6-*trimethyl* β-*methylglucoside* as needles, m. p. 78—80° (1·29 g., 83%). After further recrystallisation from ether–light petroleum (b. p. 40—60°) the substance had m. p. 79·5—80° (not raised by another recrystallisation) and $[\alpha]_D^{20}$ +34·4° in chloroform (*c*, 1·9) (Found: C, 60·1; H, 7·0; OMe, 36·5; $C_6H_5{\cdot}CO$, 31·1. $C_{17}H_{24}O_7$ requires C, 60·0; H, 7·05; OMe, 36·5; $C_6H_5{\cdot}CO$, 30·9%).

3 : 4 : 6-*Trimethyl* β-*methylglucoside.* To the benzoyl compound (1·35 g.) dissolved in 27 ml. of ethanol, 27 ml. of 0·3N-sodium hydroxide were added. After 30 minutes' boiling under reflux, water was added, and the solution concentrated to remove ethanol and extracted five times with an equal volume of chloroform. The combined extracts were dried (Na_2SO_4) and evaporated. Recrystallisation of the residue (0·92 g.) from light petroleum (b. p. 60—80°) containing a little chloroform gave the glucoside (0·79 g., 84%), m. p. 51·5—52·5° (not raised by further recrystallisation from ether–light petroleum, b. p. 40—60°), $[\alpha]_D^{20}$ −17·5° in chloroform (*c*, 2·0) (Found: OMe, 52·8. Calc. for $C_{10}H_{20}O_6$: OMe, 52·5%). After another recrystallisation the substance again had $[\alpha]_D$ −17·5°. Previous values are: $[\alpha]_D^{20}$ −20° (Haworth *et al.*, *loc. cit.*), $[\alpha]_D^{19}$ −20·9° (Peat and Wiggins, *loc. cit.*), $[\alpha]_D^{25}$ −16·4° (Sundberg *et al.*, *loc. cit.*).

3 : 4 : 6-*Trimethyl glucose.* The glucoside (1·04 g.) was hydrolysed according to Sundberg *et al.* (*loc. cit.*). A solution of the product in boiling di*iso*propyl ether, after being cooled and seeded with a specimen of the β-anomer, kindly given by Dr. G. H. Coleman of the State

University of Iowa, deposited crystals in 75% yield. Unlike Sundberg *et al.* (*loc. cit.*), we were unable to separate the material into α- and β-forms, but a small specimen was obtained with m. p. 94—97°. On admixture with Dr. Coleman's specimen (m. p. 97—98°) the m. p. was 96—98°. The remainder of our material was recrystallised from dry peroxide-free di*iso*propyl ether to give two crops. The first (0·43 g.) had $[\alpha]_D^{19}$ +67·7° (9 minutes), +77·9° (540 minutes, equilibrium value) in water (*c*, 1·7) (Found : OMe, 42·0. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). The second crop (0·18 g.) had $[\alpha]_D^{20}$ +46·5° (17 minutes), +78·2° (1140 minutes, equilibrium value) in water (*c*, 1·8). Comparison of the mutarotation curve with that of Sundberg *et al.* (*loc. cit.*) showed that this crop contained a high proportion of the β-anomer. Sundberg *et al.* give $[\alpha]_D^{25}$ +77·4° and 78·0° at equilibrium. Our material gave a single compact spot on a paper chromatogram (*n*-butanol–water), and 1 mole reduced 1·00 mole of metaperiodate (Greville and Northcote, *J.*, 1952, 1945).

BIOCHEMICAL LABORATORY,
TENNIS COURT ROAD, CAMBRIDGE.

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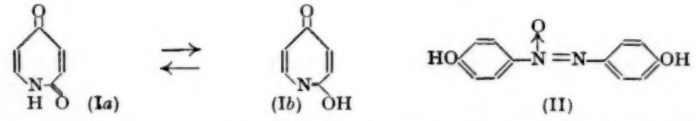
367. *The Alleged Beckmann Rearrangement of Quinone Monoxime.*

By R. A. RAPHAEL and EMANUEL VOGEL.

DURING studies on the rearrangement of oximes, Beckmann and Liesche (*Ber.*, 1923, **56**, 12) investigated that of quinone monoxime (*p*-nitrosophenol). As use of the usual acid conditions (hydrogen chloride, phosphorus pentachloride in ether) was unsuccessful the rearrangement was carried out by means of benzenesulphonyl chloride–pyridine. This treatment gave a homogeneous product to which the above workers assigned the expected seven-membered structure (I*a*) on the basis of elementary analysis and molecular-weight determination. This substance in its tautomeric imidol form (I*b*) may be regarded as an aza-γ-tropolone, and indeed some of the properties recorded by Beckmann and Liesche (*e.g.*, lack of carbonyl reactivity and solubility in alkali) gave support to this conception. It was clearly desirable therefore to re-examine this compound in the light of recently acquired knowledge of the tropolone system.



Quinone monoxime reacted violently with benzenesulphonyl chloride in pyridine, giving a tar from which the relatively pure product was readily isolated by extraction with ether. The melting points of the compound and its benzoyl derivative, its lack of carbonyl reactivity, and its solubility in alkali were found to be as described by the previous workers, but elementary analysis showed it to possess the empirical formula $C_{12}H_{10}O_3N_2$ rather than $C_6H_5O_2N$ as required by (I). It was, in fact, *pp'*-dihydroxyazoxybenzene (II), identical with an authentic specimen prepared in an unequivocal manner by peracetic acid oxidation of *pp'*-dihydroxyazobenzene (Bigiavi and Carrara, *Gazzetta*, 1923, **53**, 287). This formulation accounts for all the properties observed by the above authors and in particular for a positive Liebermann nitroso-reaction which is difficult to explain on the basis of (I).

The mechanism of formation of the azoxy-compound from *p*-nitrosophenol remains obscure. It is well known that an aromatic nitroso-compound can yield the corresponding azoxy-compound in a mild reducing medium, part being reduced to the phenylhydroxylamine which then condenses with unchanged nitroso-compound (Sidgwick, Taylor, and Baker, "Organic Chemistry of Nitrogen," 1942, p. 427; cf. Fischer and Wacker, *Ber.*, 1888, **21**, 2616). It seems difficult, however, to discern any easily oxidisable component of the present medium which would enable it to function in this manner; that pyridine should fulfil this role by conversion into its *N*-oxide is highly unlikely.

Although Beckmann and Liesche were thus in error concerning the rearrangement of quinone monoxime, there seems little doubt that from anthraquinone monoxime, they did

in fact obtain the dibenz-analogue of (I), for hydrolysis of this product readily gave *o*-amino-benzophenone-*o'*-carboxylic acid. This analogue exhibited no tropolone-like properties; it behaved as a typical keto-amide, giving carbonyl derivatives and showing no solubility in alkali.

Experimental.—Attempted rearrangement of quinone monoxime. To a solution of the oxime (9 g.) in dry pyridine (70 c.c.) benzenesulphonyl chloride (10 g.) was added slowly. The solution became warm and darkened and, on being kept overnight, deposited yellow needles of quinone monoxime benzenesulphonate. The reaction mixture was then cautiously heated on a water-bath under a reflux condenser until the inception of the violent reaction (*ca.* 20 min.). After the abatement of the reaction the cooled, dark-red solution was poured into sulphuric acid (25%; 200 c.c.), and the resulting tarry suspension well extracted with ether; the yellow ethereal extract was washed well with water and dried (Na_2SO_4). Removal of solvent gave crude *pp'*-dihydroxyazoxybenzene (II) (4·7 g.), crystallising from acetic acid in long yellowish-brown plates, m. p. 224° (decomp.) alone or mixed with an authentic sample, m. p. 224° (decomp.) (Bigiavi and Carrara, *loc. cit.*). From aqueous solvents the compound crystallised as a hydrate which readily lost water above 110° (Found: C, 62·2; H, 4·65; N, 12·25. Calc. for $C_{12}H_{10}O_3N_2$: C, 62·55; H, 4·35; N, 12·15%). The diacetate, prepared in quantitative yield by pyridine–acetic anhydride, crystallised from acetic acid in pale yellow needles, m. p. 163—164° alone or mixed with an authentic sample (Found: C 61·2; H, 4·85; N, 8·6. Calc. for $C_{16}H_{14}O_5N_2$: C, 61·15; H, 4·45; N, 8·9%). The similarly prepared dibenzoate, crystallising in pale yellow plates, m. p. 190—191°, from benzene, likewise gave no depression in m. p. on being mixed with the dibenzoate of (II) (Bigiavi and Guarducci, *Gazzetta*, 1927, **57**, 153) (Found: C, 70·95; H, 3·85; N, 6·9. Calc. for $C_{26}H_{18}O_5N_2$: C, 71·25; H, 4·1; N, 6·4%). The latter compound showed strong anisotropy at the m. p., the melt remaining turbid even at 240°; this effect is a well-known property of many azoxy-compounds.

We are indebted to Professor J. W. Cook, F.R.S., for his interest in this work, which was carried out during the tenure of a British Council Scholarship (E. V.) for which we express our thanks.

THE UNIVERSITY, GLASGOW, W.2. [*Received, January 29th*, 1952.]

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368. *An Improved Synthesis of 4-Bromo-4'-hydroxydiphenyl.*

By G. W. GRAY, J. B. HARTLEY, and BRYNMOR JONES.

DURING synthetic work 4-bromo-4'-hydroxydiphenyl was needed in quantity. Bromination of the esters of 4-hydroxydiphenyl, which according to Hazlet (*J. Amer. Chem. Soc.*, 1937, **59**, 1087; 1939, **61**, 1447) gives 4'-bromo-derivatives, led to such poor yields that the less direct method, based on the bromination of 4-nitrodiphenyl and its subsequent reduction and diazotisation, was adopted. These later steps have been much improved and can be operated on a large scale to give high yields of pure products.

Experimental.—M. p.s are corrected. Diphenyl was nitrated by the method of Bell, Kenyon, and Robinson (*J.*, 1926, 1242), except that the temperature was maintained at 86° ± 2°. In this way the yield of 4-nitrodiphenyl which crystallised from the nitration liquors was the same as that obtained previously after fractional distillation of the product. 4-Bromo-4'-nitrodiphenyl was prepared by the method of Le Fèvre and Turner (*J.*, 1926, 2045), but the yield was only 50%.

4-Amino-4'-bromodiphenyl. A mixture of 4-bromo-4'-nitrodiphenyl (81 g.), iron pin-dust (58 g.), ethyl alcohol (500 c.c.; 90%), and concentrated hydrochloric acid (29 c.c.) was stirred under reflux on a boiling-water bath for approx. 12 hours. The theoretical amount of sodium carbonate (22 g.) was added and stirring was continued for 30 minutes, whereafter a slight excess of dilute aqueous ammonia was added. After the resulting mixture had been cooled quickly, ether was added and the whole filtered (to ensure the complete removal of the amine the precipitated ferric oxide was washed with more ether). After removal of the ether from the filtrate, the warm alcoholic solution was poured into an equal volume of cold water to

precipitate the amine. This was obtained as a grey powder, m. p. 145·5° (69 g., 94%) and was virtually pure : its m. p. was unchanged by crystallisation from alcohol.

4-Bromo-4′-hydroxydiphenyl. A solution of the amine suitable for rapid diazotisation was prepared by dissolving 4-amino-4′-bromodiphenyl (60 g., 1 mol.) in glacial acetic (360 c.c.) at 90° and, while this was vigorously agitated, adding quickly 360 c.c. of a 40% (w/w) solution of sulphuric acid at 80°. Stirring was continued while the mixture was cooled to 0°. A solution of sodium nitrite (41·6 g.) in water (100 c.c.) was then added at 0° ± 1° and the mixture stirred at 0—5° until a clear solution was obtained (15—20 minutes). Urea was next added in small portions until the solution was free from nitrite (20—25 minutes). The ice-cold diazonium solution was run immediately into a vigorously stirred and boiling solution of sulphuric acid (135 c.c.; 40% w/w) in 30 minutes. The solution was added slowly at first, until suspended particles were visible in the reaction mixture, after which the rate of addition was increased. When the solution had been refluxed for 15 minutes it was cooled and diluted with an equal volume of water. The solid deposited was collected and digested with hot N-sodium hydroxide (300 c.c.). After removal of insoluble material by filtration, the orange-coloured filtrate was acidified, to give colourless 4-bromo-4′-hydroxydiphenyl, m. p. 166—167° (51 g., 85%). This material was almost pure, for crystallisation from alcohol left the m. p. at 167°.

By these procedures 43 g. (17·2%) of 4-bromo-4′-hydroxydiphenyl were obtained from 154 g. of diphenyl. These figures compare favourably with the overall yield (14·4 g., 5·8%) obtained by previous workers. Although this synthesis involves a number of steps it is reliable.

The authors are indebted to The Distillers Co., Ltd., and to Imperial Chemical Industries Limited, for financial assistance, and one of them (J. B. H.) is also indebted to Dewsbury Education Committee for a Grant which enabled him to take part in this work.

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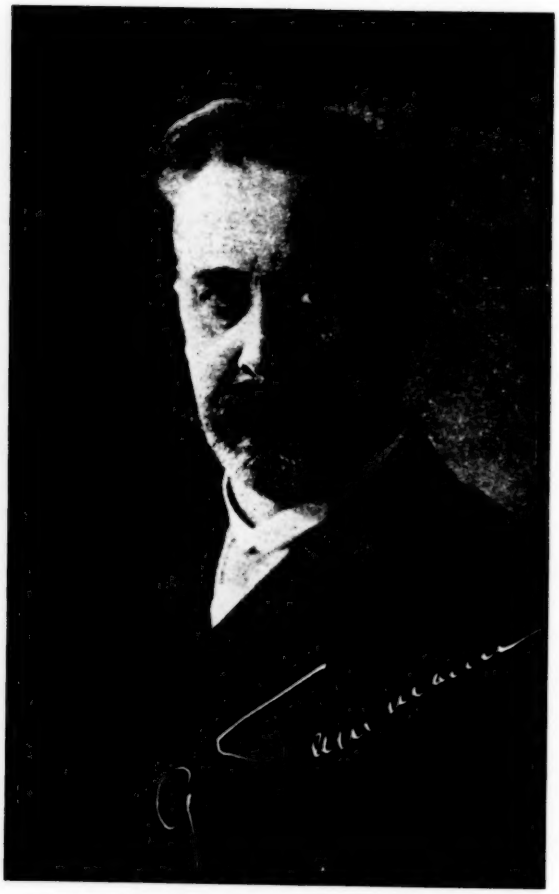


GUSTAV TAMMANN, 1861–1938.

[*To face p.* 1961.

The Tammann Memorial Lecture.

DELIVERED BEFORE THE CHEMICAL SOCIETY ON JANUARY 24TH, 1952.

By W. E. GARNER.

GUSTAV TAMMANN.

1861—1938.

GUSTAV TAMMANN was a contemporary of Ostwald, Nernst, van't Hoff, and Arrhenius, and with them laid the foundations of physical chemistry in the last years of the nineteenth century. He was born at Jamburg in 1861, just inside the borders of Russia. He was of German stock and on his father's side his forebears for some generations had resided in the Baltic States. His grandfather, Johann Tammann, was the steward of an estate near Walk, which belonged to the very influential von Berg family. His father, Heinrich Tammann, who was educated at Pernau and Dorpat, first practised as a physician at Jamburg and later at the Agricultural Institute of Gorki, under the protection of Count Frederich von Berg. His mother, Matilda Schünmann, was the daughter of a publisher who had moved to Dorpat from Lübeck. When Tammann's father died relatively young, his mother left Gorki to live with the Schünmann family at Dorpat, and it was there that Tammann was taught to read by his grandmother, Justine Schünmann.

He attended the preparatory school at Dorpat and later the Gymnasium, where usually he had the best marks in mathematics, history, and religion, though he was not so good in languages, especially Russian. A military career was open to him when General von Berg offered him a free place in the cadet school in Pleskau, but his mother declined to be separated from him. He went later to the Chemical Institute of the University of Dorpat and studied under Karl Schmidt, Lemberg, Bunge, and von Œttingen.

At that time the Dorpat-Yuriew University, which had been in existence since 1632, although essentially German in the spirit of its education, was under strong Russification. Despite a very onerous system of instruction and examination in Russian, and very large numbers of students, the University was remarkable for its academic freedom, and had a high reputation for medical, historical, and theological research. On the scientific side the emphasis was on subjects related to medicine. It is a remarkable tribute to the academic freedom of Dorpat that, in spite of this concentration in the medical field, two such important pioneers in physical chemistry as Ostwald and Tammann were able to lay the foundation of their life's work in Dorpat University.

Before Tammann had completed his final examination he was appointed second chemistry assistant under Karl Schmidt, in the place of Wilhelm Ostwald, who had obtained a professorship in Riga. In 1882 he completed his final examination and a year later submitted his "Kandidaten" thesis on the estimation of fluorine, which was published in the *Zeitschrift für analytische Chemie*. Then, on the advice of Lemberg, followed a period during which he studied plant physiology and microscopy, with a view ultimately to securing a post in an agricultural institute. He published several biochemical papers on the fluorine contents of plants and seeds, on osmotic pressures in living systems, and on fermentation processes. He finally decided, however, that agriculture was not to be his choice for a career, and that his real scientific interests lay in the borderland between physics and chemistry. His first research in this sphere was the determination of molecular weights by vapour-pressure measurements, and he published the results of his researches on this topic in Wiedemann's *Annalen (der Physik)* and in the *Mémoires* of the Academy of St. Petersburg. He could not afford to present his Doctor's thesis on this subject, since his financial means at that time were slender. Later, however, in 1887, his thesis on the Periodic Table of the elements gained him his doctorate.

After obtaining his Doctor's degree, Tammann thought that he should try to obtain a university post in Germany, since in view of his poor command of the Russian language he was unlikely to obtain promotion in a Russian university. In 1889, with this purpose in mind, he visited Germany and sought posts with Hermann von Helmholtz at the Berlin Physikalisch-Technische Reichsanstalt and with Ostwald in the flourishing school of physical chemistry at Leipzig, but was unsuccessful. His work on the vapour pressure and molecular weights in solution had been received favourably both in Germany and in Russia, but it was not along lines

then considered to be orthodox, since he was primarily interested in concentrated solutions. Ostwald, who was preoccupied with the investigations on dilute solutions which were yielding very profitable results at that time, withheld his full approval of Tammann's exploration of concentrated solutions. This was an indication quite early in his career that Tammann was beginning to strike out an independent path. Although his visit to Leipsig was unfruitful as regards securing a post, it had other important consequences since in Leipsig he became well acquainted with Nernst and Arrhenius, with whom "die Abende bei Bier verbracht werden."

Fortunately for him the promotion of Lemberg left vacant the position of first assistant at Dorpat, and the post was offered to him and he accepted it. His researches had brought him into contact with Mendeléef, with whom he had excellent relations, and Mendeléef strongly advised him to learn Russian. Opportunities for practising his Russian were limited in German-speaking Dorpat, so Tammann, during his vacations, made several visits to Russia. In 1890 he visited St. Petersburg and there met his future wife, Anna Mitcherling, whom he married in the same year, on his appointment as Dozent at a salary of 2000 roubles a year. A number of visits were made to Germany in this period, and in the Christmas vacation of 1889—1890 he worked with Nernst at Göttingen on the effects of pressure on the liberation of hydrogen by metals. After this visit he received an invitation to a professorship at Giessen, but declined the honour for financial reasons. He would have accepted had he been unmarried.

He was appointed by the Russian Government Ausserordentlicher Professor and Director of the Institute in 1892, and in 1894 he became Ordentlicher Professor. This very rapid promotion from first assistant to full professor in five years was due to his versatility and productivity in research, to his powerful personality, and to his capacity for work. His promotion at first was viewed with some misgivings by the Dorpat academic community because his research interests lay almost entirely outside the medical field, but as Tammann says laconically in his own unpublished autobiography, "after two to three years they became content." At Dorpat, he had very heavy teaching duties and he worked in the Institute alone and with students from 8 till 8, with a two-hour break at mid-day. In spite of his heavy teaching load, his period at Dorpat was most fruitful for research and he laid there the foundation of much that he did later in Göttingen.

During his tenure of the professorship at Dorpat, Tammann spent his vacations visiting various European universities and made the acquaintance of many famous physicists and physical chemists of his generation. In 1894 he paid a visit to Holland, where he met van't Hoff, Roozeboom, Kamerlingh Onnes, and Bemmelin, a visit which was to exert a very great influence in determining the direction of his researches into heterogeneous systems. He visited Nishni-Novgorod in 1896, and became interested in the oilfields of Baku. He had heard that paraffin oil was used in the canning of sardines, and carried out some investigations on the replacement of butter in part by paraffin oil in nutrition experiments with dogs, to their serious detriment. A consequence of this visit which was of more scientific significance was the isolation of some methyl derivatives of naphthalene from the crude oil. In 1897 he was in Stockholm to trace the preparations and apparatus left behind by Berzelius, and he was very largely instrumental, by his writings to the *Chemische Zeitung*, in securing the establishment of a museum in Stockholm to hold this material. In 1900 he visited Paris to study the metallurgical industries, and no doubt when there met Le Chatelier and became acquainted with his metallurgical techniques.

In the summer of 1902 Nernst enquired if he would consider an appointment as a special professor in charge of a research institute for inorganic chemistry in Göttingen. At that time there was, as a rule, only one professor of chemistry in German universities, who was an organic chemist, and branches other than organic chemistry were undeveloped. Under very considerable pressure from the German chemical industry, the German Government took steps to remedy the position. At Göttingen, Nernst was appointed as the director of an Institute of Physical Chemistry, and it was now proposed to extend this policy by the appointment of a professor of inorganic chemistry. This was the first chair of inorganic chemistry in a German university. Tammann visited Nernst to discuss the possibilities, and in the course of a walk around the walls of the ancient town, agreed to accept the invitation. He obtained permission of the Czar to give up his Russian citizenship and to accept this professorship.

He had found Göttingen to his liking when working with Nernst in 1890, and on his arrival he stated "extra Göttingen non est vivere." He remained true to this conviction, and the only move he made subsequently within his normal tenure of academic posts was to take over Nernst's own Institute of Physical Chemistry when the latter moved to Berlin. When he retired from full-time University appointment in 1930 he received an invitation to go to Riga, and this he accepted. There, very largely owing to the efforts of an old student, Dr. L. Nowack, he was generously supported by chemical industry and he vigorously continued his researches

on heterogeneous systems with the help of three to five assistants until 1937. In 1905 he became joint editor of the *Zeitschrift für anorganische Chemie.*

Gustav Tammann had three children, one son and two daughters.

Research

The tradition of Dorpat University lay in medical research, and Tammann's father and uncle were medical men, so that it was natural that his first researches were in the field of biochemistry. These in 1882 followed the analytical approach which was usual at that time, but, as his interests in the physical and physicochemical field broadened, he carried out investigations on the osmotic pressures of biological systems and on the mechanism of fermentation reactions. Although he was never to lose interest in these topics, in which he was active until 1896, his allegiance to them began to weaken when he commenced work on the vapour pressure of solutions in 1885; this was to give him a European reputation and to introduce him to men like Mendeléef, Nernst, Ostwald, and Arrhenius. These contacts gave him an interest in a wide range of subjects, the Periodic Table, electromotive force, membranes, temperature coefficients of reaction velocity, etc., which contributed in some measure to the pattern of the mosaic which was to form his life's work. His main interest was to lie in the study of heterogeneous systems, and the stimulation for this seems to have arisen from his journey to Holland in 1894. He acknowledges this source of inspiration in his book on " Heterogene Gleichgewichte " in 1924. His fundamental approach to the heterogeneous equilibria between solids and liquids, the foundations of his technical approach to crystallisation processes, and the measurement of the influence of high pressures on heterogeneous systems were all carried out at Dorpat between 1897 and 1902. He also made contributions to homogeneous systems, making use of the conception of internal pressure. In this period he showed an omnivorous capacity for absorbing the thoughts of physicists and chemists of the time, and for appreciating the experimental methods then developing in Europe; from their ideas and techniques he was able to make a choice well suited to his own genius. The main outline of the Dorpat work would appear to be the marshalling of resources in wide variety for his investigations on heterogeneous systems, and his establishment of theoretical lines of approach which were to guide his enquiries into this relatively unknown field.

At Göttingen he continued the lines of work originated at Dorpat, but, influenced by the circumstances of his appointment as Professor of Inorganic Chemistry, his interests became more practical, and he was to devote a good deal of energy to the development of inorganic chemistry. He became interested in the application of his discoveries to industrial processes. His theoretical ideas and the experimental developments of the Dorpat period were consolidated in applications to metals, glasses, silicates, and mineral chemistry. These researches created new fields of pure and applied science which were to prove of very great importance to numerous chemical industries, and a source of inspiration to many workers in pure science.

The scientific communications of Tammann and his students are very numerous, and his work would prove very difficult to review had he not written several text-books and monographs, and numerous summarising papers which describe the very complex inter-relations of the separate investigations: as a consequence of these publications, Tammann's work is very accessible, and has had a great influence on the structure of physical chemistry. The main features of his researches will be described under appropriate fields of work.

Internal Pressures and Properties of Solutions.

Tammann's determinations of the vapour pressure of salt solutions led him to state in 1885 that the molecular depressions of the vapour pressure at the same temperature are the same for similar salts: van't Hoff's paper on osmotic pressure had not yet been published. In 1887, after van't Hoff's paper appeared, he made measurements on nearly 200 salts in water at 100° and discovered clear deviations from van't Hoff's theory. These deviations, which made a deep impression on him, he explained as due to the interaction between the solute and the solvent.

The analogy between the behaviour of gaseous and dissolved substances in the theories of van't Hoff and Arrhenius focused attention on the solute and almost entirely ignored the influence of the solvent. Although this was a very valid approach for dilute solutions, Tammann recognised its limitations and devoted particular attention to the interaction of the dissolved substances with the solvent. He summarised his investigations on this topic in a monograph entitled " Über die Beziehungen zwischen der inneren Kräften und Eigenschaften der Lösungen " (1907).

His starting point was a correlation between the compressibility of water at various temperatures (Amagat) and the coefficients of expansion of aqueous solutions of electrolytes and non-

electrolytes. From the first he constructed volume–temperature relations at various constant pressures for a unit mass of pure water. From the second, he derived the volume-temperature curves, at atmospheric pressure only, of a constant mass of solvent in solutions of increasing concentrations. He showed that the effect of the solute on the expansion coefficient of the solvent was closely similar to the effect of external pressure on pure water.

Many of the properties of liquids had been explained by Laplace in terms of the conception of an internal pressure, k, the resultant of the attractive forces existing between the molecules. Tammann adopted this concept to explain the results mentioned above; he concluded that the attractive forces between the solute and solvent increased the internal pressure of the solvent, and that the increase in Δk was equal to that external pressure which was necessary to give for water the same volume–temperature curve as the solution. For both ions and neutral molecules, the increase in Δk was proportional to the concentration, and he inferred that the effects were not due solely to electrostatic forces.

A comparison of the behaviour of alcohol and water demonstrated the above inter-relations between internal and external pressure. Both the application of external pressure and the addition of solutes caused decreases in the coefficient of expansion of alcohol, whilst they caused an increase in that of water.

By pertinent use of thermodynamics, Tammann correlated the extensive data then available to him on the viscosities, heats of solution and neutralisation, optical properties, surface tensions, and vapour pressures of solutions and brought them into concordance with the changes in internal pressure of the solvent. Later he investigated the effects of pressure on the conductivity of solutions (1914), the Soret phenomenon (1914), and the influence of neutral salts on the potential of the hydrogen electrode (1925), and showed that the results were in conformity with the same idea.

Although many of Tammann's conceptions in this field have been tacitly accepted into the background of our knowledge of solutions, they have not had the same influence on the development of theory as his ideas on heterogeneous system.. The conclusions he reached were not expressible in terms of broad generalisations, simply understood, but required a knowledge of the structure of liquids and solids, which even now taxes the resources of modern statistical theory.

Heterogeneous Systems.

Equilibrium Curves for One-component Systems.—The experimental researches of Andrews and Cailletet on the equilibrium between a liquid and its vapour, and the theoretical interpretation by van der Waals of the critical point, had already been completed by the time Tammann commenced his researches on heterogeneous systems in 1895. The successful interpretation of the liquid–vapour curve encouraged Ostwald and others to apply similar ideas to the study of crystal–liquid systems. Tammann, however, pointed out that a continuous change from liquid to vapour above the critical point is possible because in both phases the molecules have random distribution. In crystals the molecules are oriented on a space lattice and accordingly the crystal and its melt will not become identical when their volumes are made equal. Therefore a terminus to the melting-point curves analogous to the critical point of the liquid–vapour curve was not to be expected. The same reasoning holds good for the equilibrium curve for two anisotropic phases.

Tammann has summarised his conclusions in this field in " Krystallisieren und Schmelzen " (1903), and in " Aggregatzustände " (1922). The first volume describes his researches at Dorpat, and the second incorporates his work at Göttingen as well. The theoretical standpoint was developed between 1895 and 1925 at a time when the methods of thermodynamics were being elaborated so that, whereas in the first volume he brings to bear on his problem the first two laws of thermodynamics in their simpler aspects, yet in the second he makes much use of the Gibbs thermodynamic potential, ζ, and also of the Nernst heat theorem. His conclusions may be indicated briefly.

At the critical point of the liquid–vapour curve, $\Delta v = 0$ and $R_p = 0$ simultaneously, where Δv is the difference between the specific volumes and R_p is the heat of transformation. He emphasises that this condition does not arise on the melting-point curve. Tammann discussed the relation between the specific volumes and the heat of crystallisation of the two phases in terms of the so-called neutral curves. The neutral curve of the specific volume is the curve drawn on the p–T plane for which $dv = 0$, and the neutral curve for the heat of crystallisation that for which $dR_p = 0$. In a discussion of the relation between these curves and the equilibrium curve for the melting point, he concludes that the diagram shown in Fig. 1 is compatible

with the Clausius–Clapeyron equation and with the customary molecular kinetic conception regarding the melting point. In this diagram the intersection of $dv = 0$ and $dR_p = 0$ lies within the closed equilibrium curve and not on the equilibrium curve itself. He points out that, although the closed curve is consistent with thermodynamics, it is not necessarily required that the closed curve should exist in actual substances. He believed, however, that the available experimental evidence was consistent with it, and he devoted considerable time and ingenuity in providing further evidence.

Fig. 2 shows one of the possible diagrams for the closed region of the crystalline phase in equilibrium along *dce* with the vapour, liquid, and amorphous phases. As will be seen in Fig. 2, the crystal–liquid curve *ce* is concave to the *p*-axis, giving a maximum. Tammann derived thermodynamic relations for its curvature, capable of experimental test, and he carried out measurements over a wide range of pressures in order to provide confirmation of the idea that a maximum exists.

FIG. 1.

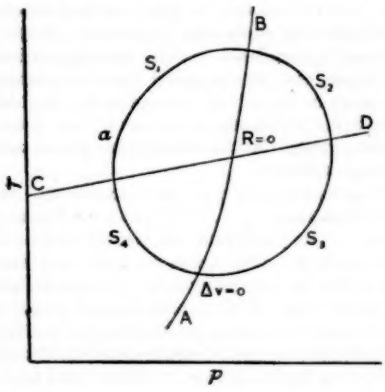
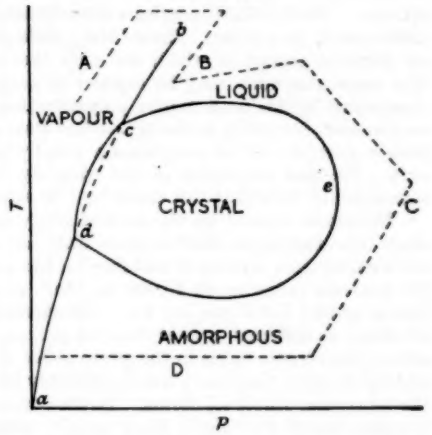


FIG. 2.



Techniques for the study of phase changes at high pressures had been developed before by Amagat and Barus. Tammann, however, extended their scope up to 4000 kg./cm.², and in rare cases up to 10,000 kg./cm.². He elaborated methods for the study of volume and heat changes and equilibrium curves inside steel vessels up to high pressures. Bridgman extended this work to still higher pressures and achieved greater accuracy in many cases. Tammann makes considerable use of Bridgman's data in his later papers.

It was confirmed, in general, that the melting-point curves were concave to the pressure axis. For ethyldimethylcarbinol, triethylcarbinol, *o*-cresol, sodium, and potassium, this type of curvature was established, but the expected maximum on the curves was not reached at 3000 kg./cm.² and Tammann concludes that, in general, the maxima must lie at very high pressures. The author lists some 40 cases and quotes some 18 cases by Bridgman, and only for a few, of which Glauber's salt was one, was a maximum actually observed. Apart from these, the maxima, if they occurred, must be in the region 20,000—30,000 atm. Although Tammann found some further confirmation of his views in the study of polymorphic systems, it is clear that his original conception of a closed melting-point curve has been only very partially confirmed. The region of the curve, Fig. 2, where the amorphous state is represented in equilibrium with the crystal phase, would obviously take geological ages to observe, so that a complete confirmation or disproof is not to be expected except possibly from geological data. The Tammann curve is therefore, at the present time, mainly of interest as a scientific speculation, which formed a high-altitude platform from which Tammann dived to investigate so many problems of practical importance.

Polymorphism.

Mitscherlich discovered the dimorphism of sulphur and mercury iodide in the early part of the nineteenth century, and since that time many other cases of dimorphism and polymorphism have been described. Lehmann distinguished two kinds of polymorphism: (1) enantiotropy, where each form has its own region of stability, and the transformation of one form into the

other is reversible, and (2) monotropy, where only one form is stable and the transformations which occur are all irreversible. Tammann pointed out that Lehmann's description was incomplete since the parameters of state alone determine whether or not a transformation will be reversible or irreversible. Thus, the circumstances in a given case might be completely changed on increasing the pressure. He therefore made a very thorough study of the conditions controlling the relative stabilities of polymorphic forms and concluded that the best criterion for stability was the thermodynamic potential. Thus, one polymorphic form is totally unstable with respect to another over the whole field of state if its ζ surface lies always above that of the other.

Tammann extended the interpretation of polymorphism by classifying polymorphs into different " thermal groups." There is one type of polymorphism for which the ζ surface of the unstable form lies above that of the stable form without intersecting it. Such pairs he designates as " members of the same thermal group "; these are considered to be composed of similar molecules having the same molecular weight and molecular structure but disposed in different lattices. Their lattice energies will be different and this will be the major factor in deciding their difference in properties. Should the ζ surfaces intersect, the polymorphs in question then belong to different groups in which not only the lattices but also the molecular units are different. The molecular units may be isomers or polymers with an appreciable heat of transformation. Associated liquids tend to give polymorphism of both types, and he suggested that the isomers or polymers occurring in the crystalline state may also exist in the liquid state as well. Liquids with a normal heat of evaporation usually give polymorphs which are members of one group only. He was interested in the meaning of molecular weight in the crystalline phase and concluded in 1914 that this could best be settled by *X*-ray methods.

Tammann opened up the field of study of the influence of pressure on polymorphism. He discovered that ice existed in three stable allotropic modifications, Ice I, Ice II, and Ice III, and determined their regions of stability on the p–T diagram. Ten years later, Bridgman extended the pressure range up to 20,000 kg./cm.^{2}, and completed the ice diagram as regards the stable forms, adding Ice V and Ice VI. Tammann returned to this field subsequently in order to test his ideas on different crystal thermal groups, and concluded that there were four, and possibly seven, monotropic forms in the group of Ice II and two monotropic forms in the group of Ice III, and he thought that there would probably be found other unstable polymorphs associated with the remaining stable ice forms. In the course of his work at high pressures he discovered polymorphic forms of phenol, silver iodide, methylene iodide, and urethane, and the number of cases was very greatly extended by Bridgman. Tammann pointed out that the transformation curves for Ice I–III and Benzene I–II give examples of transformations for which, at certain points on the p–T curves, the value of Δv is still finite, although the heat of transformation is zero, thus confirming his views that $\Delta v = 0$ and $R_p = 0$ cannot hold simultaneously on the transformation curves.

Tammann's contribution to this field was that of a pioneer in the development of the experimental technique of following polymorphic changes in steel vessels at high pressures, in developing thermodynamical methods of study, in propounding some interesting and novel ideas concerning the atomic and molecular structures of the polymorphic forms and their melts, and in raising questions concerning metastability in heterogeneous systems.

Transformation of Unstable into Stable States.

Tammann discovered new general principles which he published in the *Zeitschrift für physikalische Chemie* in 1898 and later summarised in " The States of Aggregation " (1925). He showed that there are two important factors involved in the transformation of unstable into stable states: (1) the genesis of crystallisation centres of the stable phase within the body of the unstable phase, and (2) the rates of growth of the centres of the crystallisation so formed.

Spontaneous Crystallisation.—He developed a very simple technique for the study of the crystallisation centres formed in supercooled liquids. This consisted in heating substances in closed narrow tubes to a temperature above the melting point and then suddenly cooling them in a bath at a known temperature for a fixed period. Crystallisation centres or nuclei were then formed which were not necessarily visible, owing to their slow rate of growth at the low temperature. They were, however, developable in a bath at a higher temperature in a range where centres of crystallisation did not readily form spontaneously.

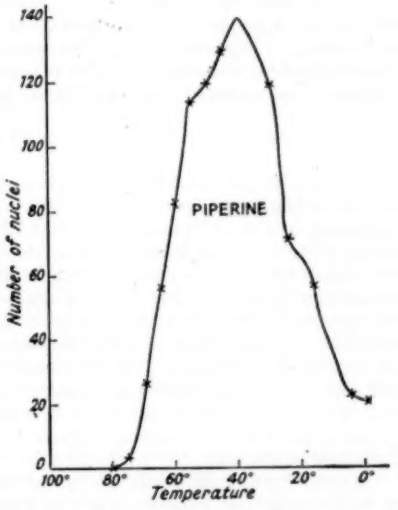
Counts of the nuclei in the case of piperine (m. p. 129°) are given in Fig. 3 as typical of his results. The now well-known result that the optimum temperature for nucleation of a melt occurs many degrees below the m. p. is apparent. He studied 16 such systems, and found

that the optimum temperature for formation of crystallisation centres ranged from 40° to 110° below the melting point. There is a zone immediately below the melting point where nucleus formation occurs extremely slowly. This is the so-called metastable region, which Ostwald had discussed in considerable detail, particularly with reference to supersaturated solutions. Tammann demonstrated that the sharp demarkation between the metastable and labile states postulated by Ostwald was illusory, since crystallisation will occur in the metastable region even close to the melting point, if sufficient time be given for the observations. He found that the number of centres formed at a given temperature was not only dependent on that temperature, but also on the duration of heating above the melting point. Thus the "anisotropic molecules" in the liquid (or on the surface of the glass), necessary for the formation of centres, are decreased by extended heating at high temperatures.

The decrease in the rate of formation of centres below the optimum temperature he ascribed to the increase in the viscosity of the liquid as it approached the glassy state. This follows since the orientation of the anisotropic molecules about a centre of crystallisation will be hindered at high viscosities.

He demonstrated experimentally that the formation of centres obeys the laws of probability. He concluded, since the probability of centre formation in a supercooled liquid is low, that in order to form a centre a relatively large number of "anisotropic molecules" must meet simultaneously in one place. He found that Ostwald's law of stages for the order of appearance of centres of polymorphic forms is not generally true.

FIG. 3.



The Linear Crystallisation Velocity.—Tammann clarified the factors governing the rate of crystallisation from undercooled liquids. He measured the crystallisation velocity, *C.V.*, in glass tubing over a range of temperatures below the melting point, and the general character of the phenomena observed was as follows. The crystallisation is slow and erratic just below the melting point, owing to the irregular growth of large crystals. At about 5° below the melting point there is a steady prismatic growth parallel to the walls of the tube, the rate of which increases with decreasing temperature up to a maximum, and in some cases to a constant value. A constant *C.V.* is only obtained over a temperature interval if the rate of crystallisation is low. As the glassy state is approached the *C.V.* decreases, becoming negligible, owing to the retardation of molecular movement.

Tammann studied the devitrification of glasses and found that their stability is inversely proportional to the rate of formation of centres of crystallisation. If initially the melt is rapidly supercooled to give the glass, and subsequently the temperature is raised, then devitrification may take place with an evolution of heat and the temperature may sometimes rise as much as 200°. This occurs with Na_2SiO_3 at 500°, when as a result of crystallisation the glass begins to glow. This phenomenon is also of significance when finely divided metals and oxides are heated.

Glasses.

As a consequence of his interest in the melting of solids and in crystallisation phenomena, Tammann investigated the properties of the amorphous state. His earlier work on the crystallisation of supercooled liquids is summarised in the previous section. In his later years, 1929 onwards, he was primarily interested in the physical changes occurring on the conversion of a glass into a liquid, particularly those occurring during the "softening interval." These researches are summarised in the monograph "Der Glaszustand" (1933). He defined the "softening interval" in terms of two temperatures which could be readily measured experimentally. This interval lies between t_g, the highest temperature at which brittleness vanishes, and t_l, the temperature at which the amorphous phase first shows the properties of a true liquid. For the latter, he chose the lowest temperature at which it was possible to obtain threads of the

amorphous material. He made use of organic molecules to establish the general principles before proceeding to borate and silicate glasses. The softening interval for simple organic and inorganic molecules was 23—29° independently of the chemical nature of the material, although the value of the mid-point t_m was a characteristic property of a chemical substance. There were, however, anomalous substances consisting of large molecules, such as high polymers, for which the softening interval was considerably greater.

He showed that many physical properties changed rapidly on passage through the softening interval, and that the changes resembled in some measure, although they were not so abrupt as, those occurring on melting. He emphasised, however, the continuous nature of the changes on passing from a glass through a liquid to a gas, and pointed out that this process could not involve a phase change. From a study of the changes in volume, specific heats, dielectric constant, optical and elastic properties, etc., he concluded that a glass could be regarded as a supercooled liquid for which the rotational movements of the molecules had been frozen. He discussed the further implications of this conclusion in later papers, in terms of his theories of polymerisation and internal pressure.

In this field, also, Tammann was a pioneer who laid the foundation of the experimental and theoretical approach which others have since followed and elaborated. Although Tammann was mainly interested in the fundamentals, he gave considerable thought to the practical applications of his researches to the glass industry, and contributed numerous papers on technological aspects to the *Glas Technische Berichte*.

Silicates.

An account of Tammann's scientific environment would be incomplete without a reference to the influence of Lemberg, who was his teacher at Dorpat. From him he acquired a geochemical outlook and he saw that much of his work on heterogeneous systems and high pressures would have practical applications in the statics and dynamics of geochemistry. Nevertheless, he entered this field only at a few points, and one of the most important of these was his work on silicates, which he began at the same time as his work on alloys. In 1904, with Wittorf he studied the action of alkali carbonates on silica, and then followed investigations on the preparation of silicates, on phase diagrams of double silicates, silicate thermochemistry, and on the interaction of nontronite and kaolin. He interested himself in the question of the constitutional formula of silicates. He found there was no appreciable lattice diffusion of silica in the crystalline lattice, and from this concluded that the term "molecule" was not applicable to any of the components of the structure of crystalline sllicates. This is in accord with the modern description of the structure of silicates.

Among his researches of direct geochemical interest was that on Wiecherts's earth structure, in which he showed experimentally in 1924 that a three-layer system was possible with silicates, sulphides, and iron–nickel, with sulphides forming the middle layer. Also, with Jander in 1925, he studied the relationships of gold and platinum to silicate melts. Although he took a great interest in it throughout his life, he was content in the main to leave the development of geochemistry to others.

Thermal Analysis.

Within the first year of Tammann's occupation of the professorship at Göttingen, he published a paper "Über die Ermittelung der Zusammensetzung chemischer Verbindungen ohne Hilfe der Analyse." In this he described his methods of thermal analysis, which are based on the measurement of cooling curves and their interpretation. The interpretation of these thermal effects in terms of Roozeboom's classical methods of representation of heterogeneous systems made it possible to construct accurate phase diagrams. As a consequence of Tammann's work, the introduction of the precise terms now in common use clarified the terminology for describing heterogeneous systems.

Thermal analysis was an important technical advance since it very largely superseded the laborious and inaccurate methods of hand-picking crystals out of a solidified mass and the subsequent gravimetric analysis. It also removed much of the vagueness which had hitherto entered into the construction of phase diagrams. It established the criteria for determining the existence of chemical compounds and solid solutions and for studying quantitatively the relations between them and the liquid phase. The changes occurring after a melt had solidified could also be followed, and compound formation detected even in the solid state. This was the beginning of the study of solid reactions.

Microscopic examination, already developed by Osmund, Sorby, and Le Chatelier, was largely used by Tammann to supplement the information gained from thermal analysis. Whereas thermal analysis gave the details of the chain of events leading to the production of an alloy, microscopic analysis gave the final composition and structure of an alloy when it was cold. To aid in this analysis, Tammann enriched our knowledge of the etching procedures to bring out the details of the microstructure of polished surfaces.

He demonstrated the existence of a " Zwischensubstanz " between the polycrystalline grains of an alloy (1922), and studied its bearing on recrystallisation. The impurities, mostly non-metallic, were concentrated at the surface of the grains, and he developed methods for the removal of the metal without gas evolution, which left behind the network of film previously covering the grains. This was done very elegantly in the case of metallic cadmium by exposure of the metal to a solution of ammonium nitrate.

In his first paper developing the methods of thermal analysis, he determined the phase diagram for sodium amalgam, which system he had previously studied in 1889 at Dorpat by freezing-point methods, and demonstrated that the metal was dissolved in mercury as atoms. With Wittorf in 1904 he examined the NO–NO_2 system. The dark blue substance which was formed from a mixture of these two gases on cooling was shown unequivocally to be N_2O_3. The borates which had proved particularly intractable by the normal methods yielded the composition of their compounds without any difficulty: the ratio of Na_2O to B_2O_3 was shown to be 1 : 2, 1 : 3, and 1 : 4, without any possibility of error. The method was successfully applied to double salts of all kinds, and in the hands of Tammann's colleagues and students, who came to him from all over the world, elucidated the structures of a very large number of metal and inorganic salt systems.

Metals.

Tammann, in his introduction to " Metallographie " (1914), mentions Roozeboom and Le Chatelier as pioneers in the application of the laws of heterogeneous equilibria, and Le Chatelier, Osmund, Roberts-Austin, Heycock, Neville, Heyn, and Weyt as the first to carry out useful experiments on mixtures of metals. However, these investigations were limited in general to the study of the beginnings of the crystallisation process, and not until the methods of thermal analysis were available was it possible to study the formation of intermetallic compounds and solid solutions with any precision. Tammann planned his investigations on a broad basis. He was a theoretician as well as an experimentalist and was able to impose a unity on the whole field which was lacking before.

One of Tammann's collaborators, G. Masing, in a paper to the memory of Tammann, explains that he saw that the field of enquiry into metals was so vast that it was not possible to make an impression on it in a reasonable time, working single-handed. He also saw that simple new techniques were needed to enable rapid progress to be made. He found these techniques in taking cooling curves and in microscopical analysis, and there soon gathered round him a large number of collaborators, which made it possible to make a very thorough survey of the metallographic field in his own lifetime.

The experimental equipment of the Göttingen school for the investigation of metals was extremely simple—a Bunsen burner, a container of cast iron, in which there was a metal crucible in the form of a tube surrounded by sand, and where necessary protected by the passage of hydrogen from a Kipp, a thermoelement, and a millivoltmeter. This was all that was needed, apart from the normal polishing equipment and a few microscopes.

Tammann's researches were summarised in his " Lehrbuch der Metallographie," which was published in 1914, 1921, 1923, and under a change of title to " Lehrbuch der Metallkünde " in 1932. These accounts enable us to trace the growth of the subject until the impacts of Tammann's work had become world wide. In the publications of the metallographic researches at Göttingen, Tammann allowed his collaborators considerable independence. They covered a very wide range of binary and, later, ternary alloy systems, including many papers on iron and steel of considerable industrial importance. An important feature of his work on metals was his interest in their physical properties. His collaborators made many investigations of the electrical conductivity, magnetism, hardness, heat capacity, heats of formation, and thermo-electromotive force of alloys and intermetallic compounds.

Formation of Compounds and Solid Solutions.—Tammann's first paper on this subject in 1906 was entitled " The Capacity of the Elements to Form Compounds," and he points out the large gaps in knowledge on this question, especially of intermetallic compounds. By 1925 he

had very considerably reduced this gap by means of 121 papers on metals from his laboratory. This interest in the Periodic Table probably originated in his contacts with Mendeléeff in the Dorpat period, and the paper in 1906 illustrates the very wide breadth of the foundation on which he organised his researches.

He has summarised the results in a number of tables which give details of the capacities of the elements to form compounds and solid solutions. He attempted to deduce the rules which govern these processes, but he finds that there is a tendency for metals to behave individually, conforming to very few rules. Elements in natural groups, that is, vertical groups of the Periodic Table, form very few compounds with one another and, when a given element forms compounds with one member of a natural group, it tends to form compounds with all members of the same group. There were, however, some exceptions to these rules.

The simplicity of the valency relations which occur in metallic salts breaks down almost entirely in the intermetallic compounds, and there is very little correspondence between the valencies for the two classes. This is illustrated by the formation of compounds of the type $NaZn_{13}$, $FeZn_7$, $NiZn_3$, etc. There was a tendency for compounds of the same valency types to be formed among members composing a natural group, but the exceptions to any rule he was able to formulate were very numerous.

According to Mitscherlich's rule concerning isomorphism, it would be expected that elements in the same vertical column of the Periodic Table would form solid solutions (mixed crystals), whilst elements far removed from one another would not do so. This is, in general, true, but it required a specially constructed Periodic Table to bring out the regularities. For example, Mn, Fe, Co, and Ni form solid solutions with Cu, Ag, and Au, which elements are brought together into close relation in Staegmüller's Periodic Table.

Cold Working and Recrystallisation of Metals.—Tammann began research with O. Faust in 1910 on the hardening of metals by cold working, and continued to publish papers on this subject until he retired in 1938. He gave a comprehensive interpretation of the processes involved in the deformation of metals and the recrystallisation processes which occur on heating, which, however, owed much to the earlier work of Ewing and Rosenheim. The unco-ordinated polycrystalline structure of a metal freshly crystallised from its melt is converted on cold working into a lamellar structure in which thin metal sheets have been produced and sheared over one another along glide planes. If a metal, such as copper, with polished surfaces be deformed above the elastic limit and examined microscopically, fine, dark, parallel lines are seen on the polished surfaces. These represent the intersection of glide planes with the surface. These planes first appear at the elastic limit of the metal and are not all produced at the same pressure, since the force which will cause gliding depends on the orientation of the individual crystallites with respect to the applied force. Tammann deduces that in the permanent deformation of crystals, parts of the crystals slide over one another along glide planes which are of two types—(1) those due to translation of one part of the crystal over another, and (2) those due to a combination of sliding, translation, and rotation of the parts of the displaced layer to form twin lamellæ.

On recrystallisation, new crystallisation centres are formed in the disorganised layers between the lamellæ which, at sufficiently high temperatures, grow and reform a polycrystalline structure. The number of new centres formed, and hence the size of the resulting crystals, depend on the amount of cold work.

Tammann investigated these phenomena from the chemical, crystallographic, and thermodynamic points of view. He studied the structure, hardness, elasticity, recrystallisation velocity, flow properties of metals, volume changes, heat evolution, conductivity, solubility, resistance to chemical attack, thermoelectric power, electromotive force, ferromagnetism, and crystallite orientation of worked metals. His textbook on Metallography contains an account of his theory, which he extended subsequently in summarising papers. In 1929 in the *Zeitschrift für anorganische und allgemeine Chemie* he summarised the results of twenty years' work on recrystallisation of metals, organic and other substances, and demonstrated the important part played in recrystallisation by thin films of impurities lying between the crystal grains.

These films, which consisted of oxides and silicates in the case of metals, or salts in the case of glacier ice, stabilise the polycrystalline structure. In the absence of such a film the usual polycrystalline structure should disappear at sufficiently high temperatures to give rise to crystals with their axes orientated in only a few preferred directions. On cold working, the continuity of the film is broken down, and therefore recrystallisation can pass the old grain boundaries. Repeated cold working, followed by recrystallisation, thus leads to the production of large crystal grains. It is of interest that the cold working of metals is used as a preliminary in one of the present-day methods of making single crystals.

Order and Disorder in the Arrangement of Atoms in Crystals of Solid Solutions of Metals. Resistance Limits.

During the First World War, Tammann studied personally the behaviour of solid solutions towards different forms of chemical attack, and found that the nature and extent of the attack depended on the method of preparation and on the pre-treatment of the alloy. This work he summarised in 1919 in the *Zeitschrift für anorganische und allgemeine Chemie*, which he dedicated to Mitscherlich, the discoverer of isomorphism. Alloys consisting of mixtures of a less noble metal with a noble metal, for example, Cu–Au or Ag–Au, when formed directly from the melt, were resistant to chemical attack by acids, oxidising agents, sulphides, etc., when the percentage of the nobler metal exceeded a resistance or parting limit. He found that alloys prepared by electrolysis did not possess this resistance. He showed that when a solid solution is prepared by slow cooling from the liquid state, the temperature is sufficiently high for the establishment of an equilibrium state among the atoms by inter-lattice diffusion, whereas in alloys prepared at room temperature by electrolysis a haphazard distribution of the atoms is obtained.

The resistance or parting limits for alloys annealed at high temperatures occur at simple ratios of the mole-fractions of the components. The value of the ratios, however, depends on the alloy and on the chemical reagent. For attack by nitric acid, the resistance limits are at ratios 1/8, 2/8, 4/8, 6/8, or 7/8 in different alloys, and Tammann was able to give a reasonable interpretation of the significance of these ratios in terms of an ordered distribution of the atoms of the solid solutions on "partial" or "super-lattices." On the other hand, a statistical examination of the distribution of atoms in a disordered state showed that no protection of a less noble by a noble metal was to be expected in such a state.

He made a thorough survey of the electromotive force and other physical properties of a number of solid solutions and found extensive support for his view that in annealed solid solutions there was an orderly distribution of atoms. He also studied the resistance limits of a number of solid solutions of inorganic salts.

In 1920 and 1922 Tammann made an important contribution to the study of the attack of metals by oxygen, the halogens, and hydrogen sulphide, where he originated the method of using the interference colours produced in the surface film to give a measure of thickness. He showed that in the attack by iodine the parabolic law held, $dy/dt = p/y$ or $y^2 = 2pt$, but that in the oxidation of metals an exponential law, $dy/dt = (1/ab)e^{-by}$, represents the increase in thickness with time.

Reactions in the Solid State.—Tammann used the method of thermal analysis to investigate with his students numerous systems involving the breakdown of solid solutions, and the formation and decomposition of chemical compounds. The importance of diffusion in the solid state in facilitating these changes was realised by him. He considered diffusion as occurring by "Platzwechsel" of the atoms, and he determined the minimum temperatures at which this exchange was possible. For metals it occurred at $0{\cdot}3T_s$, for oxides, salts, and some silicates at $\sim 0{\cdot}5T_s$, and for organic molecules sometimes as high as $0{\cdot}9T_s$, where T_s is the melting point.

He studied the phenomena which arise when pressure is applied to metal powders, and showed that alloys similar to those obtained from the melt could be manufactured by this method. This process, however, required a minimum temperature; at low temperatures even the application of very high pressures was unable to produce appreciable consolidation. These methods and ideas have been taken up fruitfully since, and one of his students, Hedvall, has paid particular attention to the interaction of solid powders and to reaction between solids.

Glacier Ice.

The flow of ice in glaciers under pressure attracted much attention towards the end of the nineteenth century, and the first theoretical explanations were based on the idea that under pressure partial melting occurred. The movement in glaciers was supposed to be due to the movement of ice grains over one another, as a result of liquefaction at points of contact. The view was put forward that a substance will melt beneath a loosely fitting piston at pressures much lower than those required with compression under a tightly fitting piston. Poynting, Ostwald, and Niggli developed this point of view by investigating various types of thermodynamic cycles to represent the process, but these led to results demonstrably mistaken, as Tammann showed. He developed methods for the study of the flow of solids under high pressures and demonstrated that ice could, in fact, flow appreciably at $-28°$ under pressures at which there can be no partial melting. His explanation is based on that which he gave for the deformation of metals, and the occurrence of very large grain size of ice crystals in arctic glacier ice he interpreted as due to recrystallisation facilitated by the destruction of the film around the grains by plastic flow.

Biochemical and Other Researches.

Investigations on the fermentation reactions involving the use of emulsin, salicin, and invertin were carried out at Dorpat between 1888 and 1896. Tammann found that the reactions did not proceed to completion or to an equilibrium state, as was the case with normal catalytic reactions. They were brought to a standstill by reaction by-products, and after removal of these products the reactions commenced again. He showed that the Arrhenius relation applied to the temperature coefficient of the natural decrease in activity of the ferments, but not to the fermentation reactions themselves. In 1904 he showed that there was a decrease in the virulence of bacteria after subjection to high pressures, and later he studied the poisoning of bacteria with metal ions.

He also worked on the permeability of membranes and concluded that the permeability could not be entirely explained in terms of their behaviour as molecular sieves, but that the solubility of substances in the membrane also played a part. Tammann used freezing-point and conductivity methods to distinguish between the isomers and polymers of metaphosphates. In 1902 this work formed almost his sole claim to the title of inorganic chemist. As examples of isomers were $Na_2(PO_3)_2$ and $Na_3(PO_3)_3$, and of polymers $Na_2[Na_4(PO_3)_6]$ and $Na_4[Na_2(PO_3)_6]$. In the cases of the last two substances he showed that alkali metal appeared in the negative ion. In his method of formulation of these complex compounds he anticipated Werner.

Appreciation

Tammann's active period of research extended from 1883 to 1938. He was a contemporary of Ostwald, Nernst, van't Hoff, and Arrhenius, and was associated with them in laying the foundations of physical chemistry. The work of his contemporaries was, however, so closely inter-related and interwoven that it is often not easy to decide to whom belongs the credit for a particular discovery. Tammann's theoretical work was much more isolated than that of his contemporaries, for he surged ahead of the advancing wave of science into regions where his contemporaries and their successors had difficulty in following him. His researches on the internal pressures of solutions and on the equilibria between the crystalline and liquid states of matter penetrated so deeply that even now the problems that interested him are still unsolved.

As Ostwald indicated to Tammann in 1889, it is, in general, most remunerative when investigators work in close contact with the scientific background of the time. It is rare that work carried out in partial isolation has the good fortune that befell the researches of both Willard Gibbs and Hittorf, which good fortune was so well merited. It would appear, in general, that the changing language of scientific thought makes it uneconomic to absorb work done ahead of the time. It is therefore problematical whether the theoretical investigations of Tammann will have any better success with a future generation of scientists than they have had with his contemporaries. Although they had a by no means negligible influence at the time, their importance would rather seem to lie in the fact that his theoretical investigations suggested to him unique methods of experimental appproach. Many of the ideas applied to practical problems appear to many of us to be disconnected flights of genius, probably because their point of origin lies beyond our ken. To Tammann his own work was a unified conception, although he has stated that he had " manches Figurchen auf Elfenbein geschnitzt."

His most important work was concerned with heterogeneous systems, and in many directions we find that he has taken the first scientific steps and has laid down the pattern of investigation or the basic idea, which his successors have accepted and further developed. His work on high pressures preceded that of Bridgman by ten years and his most striking achievements in this field were the discovery of the different forms of ice, and his interpretation of polymorphism. By his discovery of thermal analysis he made possible the construction of accurate phase diagrams and thereby initiated the rapid advances by his own students and others in the development of metallography.

Essentially his own was the formulation of the laws for systems not in equilibrium, such as those governing nucleation and the rate of crystallisation. He successfully applied these fundamental ideas to the understanding of the phenomena arising in the cold working of metals and their recrystallisation. He clarified our knowledge of the amorphous state and particularly of glasses. It is surprising how much of his work lies at the basis of the modern approach to geochemistry. By the study of chemical resistance limits, he discovered "superlattices." He employed the interference colours, formed on metals under the action of gases, to study the kinetics of heterogeneous reactions. He laid down the basis for the study of the interaction

between solid phases and showed the dependence of reactivity on diffusion in the solid state, for which he established limiting temperatures.

Tammann saw very clearly the ways in which a complicated problem could be broken down into its elements. A line of enquiry usually started in his private laboratory with an investigation with his own hands and with very simple apparatus. The problem was then handed over to his research assistants and students for further development. He had normally some 20 to 30 students working in his laboratory at Göttingen, following the lines of investigation developed first in his private laboratory. Periodically he would summarise the work of this army of investigators in papers or in monographs, and thereby make clear what had been achieved and what still remained to be done.

One of his greatest contributions to science lay in the men he trained for University and industrial research, who spread his ideas and teaching far and wide. By means of these men his impact on the development of physical chemistry was immediate in its action and at the same time was long-range in its influence. Some idea of the extent of his influence can be gathered from the Tammann "Festschrift" in the *Zeitschrift für anorganische und allgemeine Chemie*, 1926, in which over 100 students and colleagues commemorated his sixty-fifth birthday by their greetings and records of work which owed much to his inspiration.

Although Tammann lived for his work and concentrated his efforts in making the greatest possible penetration into the unknown within his life's span, he was very human in his relations with his staff and students. He was unconventional and disliked formality. His humanity showed itself during the First World War in his care for the numerous Russian students in Göttingen, whose poverty was outstanding. He had an irrepressible sense of humour which showed itself in his daily visit round the laboratory, in the Ph.D. examination, and in all kinds of unlikely places. When he was leaving Dorpat he was introduced to Archbishop Agafangel, who held out his hand to him to kiss; Tammann shook this hand vigorously, much to the amazement of the Archbishop. On the occasion of the Ph.D. examination of an American student, this student sent in his visiting card as was customary, and on entering was received with hearty roars of laughter. He had inadvertently sent in a card, on the back of which was written a couplet which he had copied from the walls of an inn the previous Sunday. Tammann, however, expected the utmost from his collaborators, and only the best would satisfy him.

He received many honours. He was honorary member of the Bunsen Gesellschaft, of the Deutschen Gesellschaft für Metallkunde, of the British Institute of Metals, an Honorary Fellow of the Chemical Society, and was the recipient of the Bunsen, Heyn, and Karl Lueger Prizes. He was a member of many Academies. At the age of 75 he was awarded by Adolf Hitler the Adlerssheld of the Deutsches Reich.

Acknowledgment is made to Herr Gustav Augenheister for the loan of his grandfather's unpublished autobiography, to the appreciation of Tammann's work by Professor W. Biltz in the *Zeitschrift für anorganische und allgemeine Chemie*, 1931, and to obituary notices by Professor G. Masing in *Die Naturwissenschaften*, 1939, and in the *Zeitschrift für Elektrochemie*, 1939. My thanks are also due to Dr. W. J. Dunning for suggestions made after reading the manuscript.

Some Recent Developments in the Chemistry of Free-radical Reactions in Solution.

TILDEN LECTURE, DELIVERED BEFORE THE SOCIETY AT THE UNIVERSITY, LEEDS, ON NOVEMBER 22ND, 1951, AND AT BURLINGTON HOUSE ON DECEMBER 13TH, 1951.

By D. H. HEY, D.Sc., F.R.I.C.

IT is now exactly fifty years since Lapworth [1] in this country and Noyes [2] in America put forward the view that electrolytic dissociation or ionisation played an important part in the reactions of organic compounds. In this way they provided a theoretical basis common to both inorganic and organic chemistry which helped to check the divergent paths which these two branches of the subject were tending to follow in the latter part of the nineteenth century. The subsequent introduction of the electronic theories of Lewis and Langmuir enabled the earlier hypothetical speculations to be translated into terms which were more closely related to physical reality and thereafter, very largely as a result of the work of the schools associated with the names of Robinson and of Ingold, a comprehensive theory of reaction mechanisms was developed. This theory, with but few adjustments, has now incorporated the more recent quantum-mechanical concepts of resonance which place it on a more fundamental and semi-quantitative basis. About twenty-five years ago a more intensive study of the photochemical and pyrolytic reactions of organic compounds, and in particular the experimental proof of the free existence of the simple alkyl radicals by Paneth and others, showed that in many reactions ionic dissociation was not involved and that the reacting entities were electrically neutral radicals or atoms resulting from the symmetrical fission of a covalent bond. These two types of reaction are now conveniently classified as heterolytic and homolytic reactions, respectively, according to the terminology introduced by Ingold.[3] Subsequent developments have established the existence of numerous reactions involving atoms and free radicals, both in the gaseous state and in solution, but a more complete understanding of this field, especially for reactions in solution, has hitherto been seriously hampered, except perhaps in the field of polymerisation, by a lack of accurate quantitative information.

The general pattern of free-radical reactions in solution has now become clear and the majority of such reactions can be classified as either substitution or replacement reactions, *e.g.*,

(i) $$R\cdot + AB \longrightarrow RA + B\cdot$$

or addition reactions involving a chain-reaction mechanism, *e.g.*,

(ii) $$R\cdot + X\cdot CH{:}CH_2 \longrightarrow X\cdot \underset{|}{C}H\cdot CH_2R$$

(*a*) $$X\cdot \underset{|}{C}H\cdot CH_2R + RY \longrightarrow X\cdot CHY\cdot CH_2R + R\cdot$$

or (*b*) $$X\cdot \underset{|}{C}H\cdot CH_2R + X\cdot CH{:}CH_2 \longrightarrow X\cdot \underset{|}{C}H\cdot CH_2\cdot CHX\cdot CH_2R, \text{ etc.}$$

The reaction (ii, *a*), which results in the direct addition of RY to $X\cdot CH{:}CH_2$ may, under favourable conditions, be replaced by an alternative course (ii, *b*), in which the intermediate free radical $X\cdot \underset{|}{C}H\cdot CH_2R$ reacts with the ethylenic molecule $X\cdot CH{:}CH_2$ rather than with the molecule RY and gives rise to addition polymerisation. Free-radical substitution or replacement reactions are usually characterised by a *low degree of specificity* as revealed, for example, in homolytic aromatic substitution or in the atomic chlorination of straight-chain aliphatic acids. On the other hand, free-radical addition reactions normally show a very *high degree of specificity*, similar to that shown in heterolytic addition reactions, which leads to unidirectional reaction. This is revealed, for example, in the peroxide-induced addition of hydrogen bromide to unsymmetrical ethylenic systems and in the large number of addition reactions of halogeno-alkanes studied by Kharasch.[4] The low specificity of the substitution reactions is in keeping with the electrical neutrality of the free radical R·, which reacts with the unperturbed molecule AB in the absence of long-range coulombic forces and molecular polarisation. The high specificity of the addition reactions may be attributed to the differential stabilities of the alternative intermediate free radicals, which can vary with structure within very wide limits. It is important to recognise, however, that the products formed in either type of homolytic

reaction need not necessarily be different from those formed in the corresponding heterolytic reaction. An interesting example of the formation of the same product by two different mechanisms has been provided by Kharasch and Fuchs [5] in the addition of thiols to methyl acrylate. These reactions, which are catalysed by *either* a strong base *or* a free radical, may be represented as follows :

$$\text{(I)} \quad RS^- + CH_2{:}CH{\cdot}CO_2Me \longrightarrow [RS{\cdot}CH_2{\cdot}CH{\cdot}CO_2Me]^-$$
$$[RS{\cdot}CH_2{\cdot}CH{\cdot}CO_2Me]^- + RSH \longrightarrow RS{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Me + RS^-$$
$$\text{(II)} \quad RS{\cdot} + CH_2{:}CH{\cdot}CO_2Me \longrightarrow RS{\cdot}CH_2{\cdot}\dot{C}H{\cdot}CO_2Me$$
$$RS{\cdot}CH_2{\cdot}\dot{C}H{\cdot}CO_2Me + RSH \longrightarrow RS{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Me + RS{\cdot}$$

Product analysis by itself cannot therefore always be relied upon as a certain guide to mechanism. In the homolytic reaction (II) the product also contains compounds formed from two or more molecules of methyl acrylate for each molecule of thiol (reaction ii, *b*).

Another feature of homolytic reactions which has now become clearer is the recognition of the possibility, under suitable experimental conditions, of the *simultaneous* occurrence of homolytic and heterolytic processes. This is illustrated, for example, in the work of Wibaut [6] on the influence of temperature on the orientation of the products in the halogenation of aromatic compounds, and the same principle appears to be evident in the recent work of Klapproth and Westheimer [7] on aromatic mercuration. These workers have shown that many of the apparent anomalies in the orientation of the products in aromatic mercuration become more readily understood if a distinction is made between mercuration with ionised mercuric salts in strong acid solution on the one hand and mercuration with the largely undissociated mercuric acetate in non-polar solvents on the other. In the former case, *e.g.*, with mercuric perchlorate in aqueous perchloric acid, the usual orientation effects for electrophilic substitution are observed, as is shown in the following figures for the mercuration of nitrobenzene, whereas in the latter case the orientation effects are much less pronounced, which is one of the characteristics of a homolytic process :

Mercuration of nitrobenzene.

Experimental conditions	*o*- + *p*-Substitution, %	*m*-Substitution, %
$Hg(ClO_4)_2$ in 60% $HClO_4$ at 23°	11	89
$Hg(ClO_4)_2$ in 40% $HClO_4$ at 95°	37	63
$Hg(OAc)_2$ in excess of $Ph{\cdot}NO_2$ at 95°	52	48
$Hg(OAc)_2$ in excess of $Ph{\cdot}NO_2$ at 150°	57	43

In both of these examples there is clearly no sharp line of demarcation between the heterolytic electrophilic type, which shows the typical pronounced orientation effects, and the homolytic type in which these effects are smoothed out. This smoothing out or levelling effect has also been observed in other ways. Szwarc, Leigh, and Sehon,[8] in an investigation on the influence of aromatic substitution on the C–Br bond dissociation energy in a series of substituted benzyl bromides, have shown that substitution of a hydrogen atom in the ring by chlorine, bromine, methyl, nitro- or cyano-groups, results in comparatively small changes in the activation energy of the process $X{\cdot}C_6H_4{\cdot}CH_2Br \longrightarrow X{\cdot}C_6H_4{\cdot}CH_2{\cdot} + Br{\cdot}$, in sharp contrast to the effect of these substitutents on comparable ionic reactions.

This characteristic absence of specificity in homolytic substitution or replacement reactions is nowhere more clearly demonstrated than in homolytic aromatic substitution. The well-known clearly-defined orientation effects observed in substitution by electrophilic and nucleophilic reactions are here so effectively damped down that it becomes important to redefine the terms *o*/*p*-direction and *m*-direction by reference to the statistical ratio of 60% *o*/*p*-substitution and 40% *m*-substitution. Substituent atoms or groups which give rise to more than 40% substitution at the *m*-position are termed *m*-directing; those giving less than 40% are termed *o*/*p*-directing. On this basis all the reactions which are to be found in the earlier experimental work on homolytic aromatic substitution are examples of *o*/*p*-substitution. In homolytic aromatic substitution, however, the subdivision into *o*- and *p*-substitution on the one hand, and *m*-substitution on the other, has no real justification, and these conventional terms are retained here only in order to direct emphasis to the characteristic differences between the results obtained in heterolytic and homolytic substitution. The quantitative figures available to date must be accepted only as rough approximations, but more accurate quantitative data in this

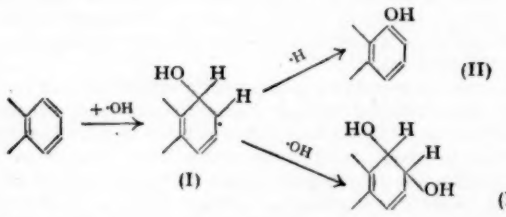
field have recently become available in the work of Weiss[9–13] and his collaborators on substitution reactions with the hydroxyl radical, derived from either Fenton's reagent or the action of ionising radiations on aqueous solutions. In both cases the reactions with nitrobenzene and with chlorobenzene show that the nitro-group and the chlorine atom are *o*/*p*-directing, this term being used in the conventional sense as defined above, as shown in Table 1.

The hydroxylation of benzoic acid by means of free hydroxyl radicals produced by *X*-rays has also been reported by Stein and Weiss,[10] who recorded the formation of *o*-, *m*-, and *p*-hydroxybenzoic acids in the approximate ratio 6 : 4 : 10. The irradiation of ferric ion-pair complexes has been reported by Bates, Evans, and Uri,[14] and their reaction product was said to include *o*-, *m*-, and *p*-hydroxybenzoic acids in the approximate ratio 2 : 2 : 1.

TABLE 1. *Action of hydroxyl radical on nitrobenzene and on chlorobenzene.*

Source of radical	Aromatic compound	pH	Yield of isomerides, %: *ortho*	*meta*	*para*
$FeSO_4$–H_2O_2	$Ph{\cdot}NO_2$	—	25—30	20—25	50—55
$H_2O \rightsquigarrow H{\cdot} + {\cdot}OH$	,,	2	34·5	31	34·5
,,	,,	6	35·5	29	35·5
,,	,,	12	27·5	27	45·4
$FeSO_4$–H_2O_2	PhCl	—	40—45	20—25	20—25
$H_2O \rightsquigarrow H{\cdot} + {\cdot}OH$	,,	2	25—30	30—35	35—40
,,	,,	6	15—20	20—25	50—60
,,	,,	12	35—40	20—25	35—40

The process of aromatic hydroxylation by means of hydroxyl radicals is of special interest on account of its biological implications in the metabolism of drugs and toxic substances. The results of the biological hydroxylation of simple aromatic compounds have been reviewed by Smith,[15] and these show that in derivatives carrying the classical *o*/*p*-directing groups the hydroxylation is found to take place at the *o*- and *p*-positions, while with the classical *m*-directing group NO_2 hydroxylation takes place at the *o*-, *m*-, and *p*-positions.[16] While there does not appear to be any direct evidence on the biological hydroxylation of benzoic acid, it may be mentioned that Lederer [17] has reported the occurrence of *o*-, *m*-, and *p*-hydroxybenzoic acids as normal constituents of the urine of pregnant mares. These experimental observations, which reveal a close parallel with the work of Weiss, are readily explicable on the basis of a free-radical mechanism, which in biological systems involves not necessarily the free hydroxyl radical but a precursor such as the sulphate radical ion as in the Elbs reaction.[18] Smith [15] has further pointed out that with aromatic compounds in biological systems either phenol or diol formation can occur (II or III) and both can arise from a common intermediate radical (I), the stability of which would largely control whether it would eject a hydrogen atom or combine with another hydroxyl radical. The former process would be expected to take place with simple benzene derivatives, and the latter with the more complex polycyclic hydrocarbons, which would give rise to more stable intermediate radicals owing to the additional resonance energy associated with the fused aromatic structures.



Although the general characteristics and significance of homolytic aromatic substitution reactions are thus becoming clearer, the further development of the subject is restricted by the dearth of accurate quantitative data. This is particularly evident in the substitution reactions in which aryl radicals take part as a result of the reactions of certain diazo-compounds and of acyl peroxides. Many of these reactions lend themselves very well to quantitative study. In an attempt to provide such data a detailed investigation has now been initiated into the quantitative aspects of the reactions of aryl radicals on a wide range of aromatic compounds.

In the earlier qualitative work substitution by aryl radicals was reported to have taken place at the *o*- and *p*-positions only, but in a homolytic substitution process the occurrence of some substitution at the *m*-position might also be expected. It was necessary, therefore, to carry out a series of reactions with aryl radicals (Ar), derived from several different sources, and an aromatic compound (PhR), and to submit the products of these reactions ($Ar{\cdot}C_6H_4R$) to a method of analysis which would allow the proportion of the *m*-isomeride to be estimated. With regard to the directing influence of the nitro-group, the method first employed was based on a bromometric titration of the mixed bases formed on reduction of the mixed nitrodiphenyls.[19] Since the *m*-amine reacts with three molecular proportions of bromine, whereas the *o*- and the *p*-isomeride react with only two molecular proportions, the method provides a means of estimating the ratio $m/(o + p)$. The analytical procedure was tested with synthetic mixtures and shown to be reliable, but it was found that the aryl radical could not be phenyl because, whereas 2- and 3-aminodiphenyl react normally, 4-aminodiphenyl cannot be titrated with a bromide–bromate mixture without undergoing oxidation. The experimental work was therefore carried out with the *p*-bromophenyl and *p*-tolyl radicals, and four sources of the free radical were used in each series, namely, the diazoate, nitrosoacylarylamine, dimethyltriazen, and the acyl peroxide. The results of these reactions, summarised in Table 2, show that the

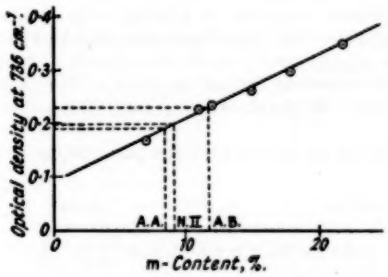
TABLE 2. *Action of aryl radical on nitrobenzene.*

Source of radical, *p*-R·C_6H_4·	*meta*, %: R = Br	R = Me	Source of radical, *p*-R·C_6H_4·	*meta*, %: R = Br	R = Me
Diazoate, *p*-R·$C_6H_4{\cdot}N_2{\cdot}ONa$	12·5	9·4	Dimethyltriazen, *p*-R·$C_6H_4{\cdot}N_2{\cdot}NMe_2$	21·7	7·0
	12·3	8·3		28·6	8·5
		9·1		24·5	
Nitrosoacylarylamine, *p*-R·$C_6H_4{\cdot}N_2{\cdot}OAc$	11·9	8·7	Acyl peroxide (p-R·$C_6H_4{\cdot}CO_2)_2$	11·8	9·5
	12·7	8·0		11·6	9·2
			Average	(12·1)	(8·6)

p-bromophenyl radical enters the nitrobenzene nucleus at the *m*-position to the extent of 12·1%, while for the *p*-tolyl radical the figure is 8·6%.

The results are thus qualitatively in agreement with those of Weiss for the hydroxyl radical, and the figure for *m*-substitution in these reactions is substantially independent of the source of

FIG. 1.



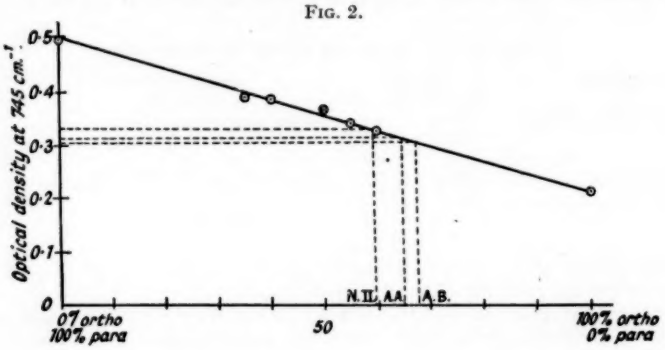
the aryl radical, which may be interpreted as evidence for a common mechanism to all four reactions involving the aryl radical as the substituting agent. The anomalous results obtained with 1-*p*-bromophenyl-3 : 3-dimethyltriazen have been shown to be due to the rearrangement of *p*-bromobenzenediazochloride, formed by the action of hydrogen chloride on the triazen, into *p*-chlorobenzenediazobromide: the bases obtained on reduction of the reaction product are thus a mixture of 4-bromo- and 4-chloro-aminodiphenyls in unknown proportions, which leads to an abnormal result in the bromide–bromate titration.

The information thus obtained, which establishes the occurrence of substitution at all three positions with reference to the nitro-group, does not provide the proportions in which all three isomerides are formed, and it gives no information on the influence of the substituent nitro-group on the activation or deactivation of the nucleus as a whole. To obtain the complete picture it is necessary to pursue two parallel lines of investigation, as was in fact done by Ingold and his collaborators [20–21] for electrophilic aromatic substitution more than twenty years ago,

namely, (*a*) the determination of the proportions in which each of the three isomerides is formed, and (*b*) the determination of the rate of the total substitution reaction relatively to that of benzene. By means of infra-red spectroscopy it has now been possible to obtain an accurate assessment of the directing influence of both the chlorine atom and the nitro-group, and by means of a series of competitive reactions the activating or deactivating influences at work have been quantitatively assessed.

Infra-red spectroscopy was first applied to the reaction product obtained from the action of phenyl radicals on nitrobenzene.[19] Such a product would be expected to provide results which should be in close agreement with those already obtained by chemical analysis for the corresponding reactions with the *p*-bromophenyl and *p*-tolyl radicals. A preliminary study of the infra-red spectra of the three isomeric nitrodiphenyls in nitromethane showed that characteristic bands for each isomeride occurred within the region 710—810 cm.$^{-1}$, but that there was considerable overlapping. It was found, however, that the absorption at 736 cm.$^{-1}$ provided a direct measure of the *m*-isomeride in artificial mixtures of the three isomerides, and the variation in optical density at this wave number with the content of the 3-isomeride is shown in Fig. 1. The variation in optical density at 736 cm.$^{-1}$, due to changes in the *o*- and

FIG. 2.



p-content, was shown to be comparatively small. By means of this graph it was possible to estimate the extent of substitution at the *m*-position with respect to the nitro-group. The proportion of substitution at the *o*- and *p*-positions was obtained in similar manner by measurement of the optical density at 745 cm.$^{-1}$, which was shown to be particularly sensitive to the *o* : *p* ratio. Fig. 2 shows the observed optical densities of the pure *o*- and *p*-isomerides and of mixtures of the two, and from this graph the *o* : *p* ratio of a mixture of unknown composition can be estimated.

The results thus obtained for the products of the phenylation of nitrobenzene are as follows:

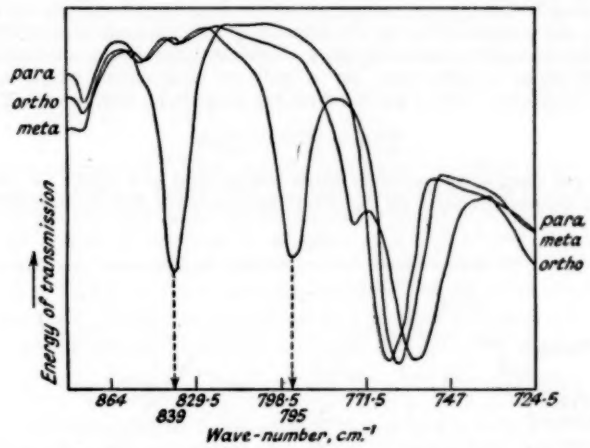
Source of Ph radical	Nitrodiphenyls, %: *ortho*	*meta*	*para*
Na benzenediazoate (N.H.)	54 ± 4	9 ± 2	37 ± 4
Benzoyl peroxide (A.A.)	59·5 ± 4	8·5 ± 2	32 ± 4
,, ,, (A.B.)	59·5 ± 4	11·5 ± 2	29 ± 4

These results provide, not only confirmation of the results previously obtained by chemical analysis, but also further indication of the independence of the orientation on the source of the phenyl radical. During the course of this work, De Tar and Scheifele [22] reported results on the phenylation of nitrobenzene, using benzoyl peroxide, benzenediazohydroxide, and nitrosoacetanilide as their source of the phenyl radical and employing measurement of the ultra-violet absorption for the determination of the proportions of the isomerides formed. Their results are in general agreement with those reported above, but a comparison of the two investigations shows the superiority of the infra-red technique in this particular instance.

A similar investigation was carried out on the product obtained by the action of phenyl radicals on chlorobenzene, both the Gomberg reaction and benzoyl peroxide being used as the source of the phenyl radical.[23] In the preliminary study of the infra-red absorption of the three isomeric chlorodiphenyls in nitromethane solution it was found that the *m*- and *p*-isomerides possessed characteristic bands in the region 11—15μ, but the corresponding band

for the *o*-isomeride was very close to a strong band common to all three isomerides and would probably be of little value for quantitative estimation (Fig. 3). Measurements were made in nitromethane solution, the 795 cm.$^{-1}$ and 839 cm.$^{-1}$ bands being used to estimate the *m*- and the *p*-content, respectively, the *o*-content being derived by difference. A typical curve for such an experimental mixture is shown in Fig. 4. The reliability and accuracy of the method are illustrated in Table 3, and the analytical results for a series of nine reaction products, obtained from either sodium benzenediazoate or benzoyl peroxide, are shown in Table 4.

FIG. 3.



In the parallel investigation on the determination of the activating or deactivating influence of the substituent atom or group, two lines of approach are possible, namely, the direct measurement of the velocity constants for attack on the substituted and unsubstituted compounds, and the method of competitive experiments in which the ratio of the velocity constant for attack

TABLE 3. *Infra-red analysis of mixtures of chlorodiphenyls.*

Solution	Percentage of chlorodiphenyls: *ortho*	*meta*	*para*
(i) Found	42·36	30·57	27·07
Calc.	39·14	32·14	28·72
(ii) Found	48·80	29·47	21·73
Calc.	44·29	32·47	23·24
(iii) Found	—	62·42	37·58
Calc.	—	61·90	38·10

TABLE 4. *Phenylation of chlorobenzene.*

Reaction	Percentage of chlorodiphenyls: *ortho*	*meta*	*para*
Gomberg, (i)	64·48	21·30	14·22
,, , (ii)	65·78	20·55	13·67
,, , (iii)	63·37	22·72	13·90
,, , (iv)	64·48	22·23	13·09
Benzoyl peroxide, (v)	62·82	24·56	12·62
,, , (vi)	61·36	24·99	13·65
,, , (vii)	57·62	27·08	15·29
,, , (viii)	60·27	25·89	13·84
,, , (ix)	59·51	26·98	13·51

on a pair of compounds (X and Y) is obtained by analysis of the mixed product formed when a mixture of the two compounds of known composition is allowed to react in a homogeneous medium with a limited quantity of the substituting agent. The ratio of the velocity constants k_x/k_y or ${}^{x}_{y}K$ is equal to the ratio of the amounts of the two products formed from an equimolar

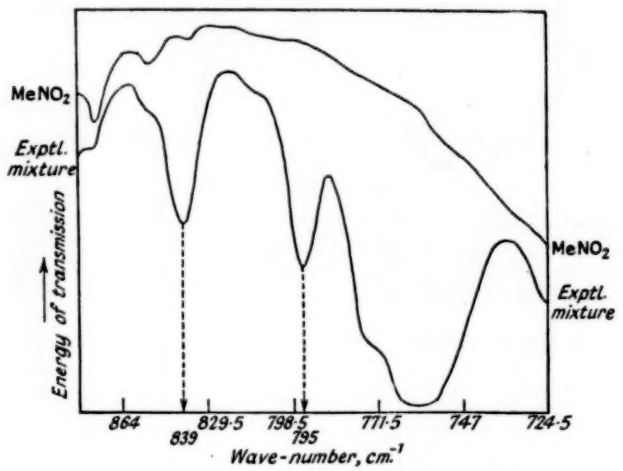
mixture of the two components X and Y provided (*a*) that the excess of the two components over the attacking reagent is large, so that the molar composition of the mixture is not appreciably disturbed by the unequal rates of disappearance of the two components, and (*b*) that the substitution reactions under investigation are of the same kinetic order.

For the reactions under investigation the method of the direct kinetic approach is of uncertain value because it is probable that in most cases it is not the actual substitution reaction which is the rate-determining stage. It is thus necessary to use the method of competitive reactions on the lines employed by Ingold and his collaborators [20, 21, 24, 25] for electrophilic substitution. The competitive method, moreover, possesses two special advantages in that (i) it allows measurements to be carried out with a solid component provided it is sufficiently soluble in the second component to give a solution of the required concentration, and (ii) by means of successive estimations with two pairs of reactants containing one reactant in common, it is possible to derive a rate ratio for a pair of components which cannot be satisfactorily compared directly. Thus, for the three reactants ArH, ArX, and ArY, we have :

$$\frac{ArX}{ArH}K = \frac{ArX}{ArY}K \times \frac{ArY}{ArH}K$$

There are several alternative reactions which can be used as a source for the aryl radical as outlined above in the parallel work on the orientation problem, but in competitive experiments

FIG. 4.



it is essential to use a homogeneous or one-phase system in order to eliminate purely mechanical factors such as rate of stirring, and for the present purposes the reactions of benzoyl peroxide were chosen. These reactions, which may be represented thus :

Main reaction : $(Ph{\cdot}CO_2)_2 + ArH \longrightarrow PhAr + Ph{\cdot}CO_2H + CO_2$
Side reaction : $(Ph{\cdot}CO_2)_2 + ArH \longrightarrow PhH + Ph{\cdot}CO_2Ar + CO_2$

are usually clean and it has been generally found possible to account for about 85—90% of the reagent as identified products. In all cases it is first necessary to remove benzoic acid and benzoates, which are formed as by-products.

The experimental procedure requires a method for the quantitative analysis of the two products, PhAr and PhAr′, which result from the attack of ArH and Ar′H by the phenyl radical. Three analytical methods were evolved, nitrobenzene, chlorobenzene, or pyridine, being used as one reactant of each pair.[23, 26] The products from the reactions with nitrobenzene were analysed by quantitative reduction with titanous chloride under special experimental conditions previously developed and tested with artificial mixtures of known composition. The products from reactions with chlorobenzene were analysed for chlorine by a micro-Carius method, and the products from the reactions in which pyridine was used as one of the components were analysed by separation into neutral and basic fractions. With certain combinations of

reactants, for example PhCl and Ph·NO_2, two independent methods of analysis are available. Time does not permit mention of certain experimental difficulties which were encountered with various pairs of reactants and subsequently overcome. Four reactants were used, namely, benzene, nitrobenzene, chlorobenzene, and pyridine, which give rise to six pairs. The experimental results are summarised in Table 5.

TABLE 5. *Direct rate ratios from competitive experiments.*

Reactants: X	Reactants: Y	Expt. no.	${}^{x}_{y}K$		Reactants: X	Reactants: Y	Expt. no.	${}^{x}_{y}K$	
Ph·NO_2	PhH	1	11·57	> 4·17	PhCl	Ph·NO_2	12	0·358	0·361
,,	,,	2	23·27		,,	,,	13	0·364	
,,	,,	3	5·21		C_5H_5N	PhH	16—23	1·04	
,,	,,	11	4·17		PhCl	C_5H_5N	24—26	1·15	
PhCl	PhH	14	1·21	1·31	Ph·NO_2	C_5H_5N	29—30	3·95	
,,	,,	15	1·41						

The direct determination of ${}^{Ph\cdot NO_2}_{PhH}K$, *i.e.*, the rate ratio for nitrobenzene and benzene, was not wholly satisfactory because of the comparatively high volatility of diphenyl, some of which was always lost during the removal by distillation of the excess of nitrobenzene. Modifications in the working-up procedure, designed to eliminate this loss, account for the very variable results. The results can be accepted as giving a *maximum* value for ${}^{Ph\cdot NO_2}_{PhH}K$. As explained above, however, it is possible to derive indirect values for ${}^{Ph\cdot NO_2}_{PhH}K$ by employing chlorobenzene in the first instance and pyridine in the second as a common reference compound. The rate ratios measured were therefore ${}^{PhCl}_{PhH}K$, ${}^{Ph\cdot NO_2}_{PhCl}K$, and ${}^{PyH}_{PhH}K$, ${}^{Ph\cdot NO_2}_{PyH}K$, whence

$${}^{PhCl}_{PhH}K \times {}^{Ph\cdot NO_2}_{PhCl}K = {}^{Ph\cdot NO_2}_{PhH}K \text{ and } {}^{PyH}_{PhH}K \times {}^{Ph\cdot NO_2}_{PyH}K = {}^{Ph\cdot NO_2}_{PhH}K$$

The following rate ratios (Table 6) can be derived from pairs, or from groups of three, of the directly determined rate ratios in Table 5, each group of two or three providing two new values for K.

TABLE 6. *Derived rate ratios from competitive experiments.*

Reactants: X	Reactants: Y	${}^{x}_{y}K$ Direct	${}^{x}_{a}K{}^{a}_{y}K$ Derived	${}^{x}_{a}K{}^{a}_{b}K{}^{b}_{y}K$ Derived	Reactants: X	Reactants: Y	${}^{x}_{y}K$ Direct	${}^{x}_{a}K{}^{a}_{y}K$ Derived	${}^{x}_{a}K{}^{a}_{b}K{}^{b}_{y}K$ Derived
Ph·NO_2	PhH	> 4·17	3·63	3·31	C_5H_5N	PhH	1·04	1·14	0·92
			4·11	4·50				1·05	1·30
PhCl	PhH	1·31	1·50	1·48	PhCl	C_5H_5N	1·15	1·26	1·44
			1·20	1·21				1·42	1·24
PhCl	Ph·NO_2	0·361	0·29	0·29	Ph·NO_2	C_5H_5N	3·95	4·00	3·67
			0·31	0·32				3·19	3·50

The values selected for ${}^{Ph\cdot NO_2}_{PhH}K$ and ${}^{PhCl}_{PhH}K$ on the basis of the above results are 4·0 and 1·44, respectively, the latter value being based on ${}^{PhCl}_{Ph\cdot NO_2}K = 0{\cdot}361$, which is regarded as the most reliable figure, by multiplying by 4. For electrophilic substitution (nitration) the corresponding figures are $\sim 10^{-4}$ and 0·033.

De Tar and Scheifele [22] have recently reported a qualitative competitive reaction of nitrosoacetanilide with a mixture of benzene and chlorobenzene. They, too, found that the chlorobenzene was preferentially attacked and they comment on the fact that in electrophilic substitution Bird and Ingold [25] found that benzene underwent nitration with nitric acid-acetic anhydride 30 times faster than did chlorobenzene. Nearly twenty years ago Grieve and Hey [27] allowed toluene and nitrobenzene (both in excess) to compete for phenyl radicals derived from sodium benzenediazoate, and reported that the yield of nitrodiphenyls was four times as great as the yield of methyldiphenyls.

The results outlined above have established that both the nitro-group and the chlorine atom are *activating* in homolytic aromatic substitution, but the effects shown are very much *smaller in magnitude* than those encountered in electrophilic substitution. This is in agreement with the general pattern of homolytic reactions, which are free from the powerful electrostatic forces which dominate heterolytic reactions. The neutral radical approaches the site of the reaction not only without experiencing either electrostatic attraction or repulsion, but also without causing any electronic perturbation in the molecule to be attacked.

The quantitative information thus made available enables the results to be combined and expressed more explicitly in terms of *partial rate factors*. This concept, first introduced by Ingold *et al.* in 1931 [21] for electrophilic aromatic substitution, gives a quantitative expression for the influence of a substituent atom or group on reactivity in relation to substitution at an individual nuclear carbon atom. If the rates of homolytic substitution are expressed in terms of the rate of substitution at any one position in the aromatic nucleus, the rate for benzene as a whole becomes 6 and that for nitrobenzene as a whole 24, and, provided the proportions are known in which the *o*-, *m*-, and *p*-isomerides are formed, the rates of substitution at each position in nitrobenzene can be calculated. The partial rate factors designated ${}^{PhX}_{PhH}F_o$, ${}^{PhX}_{PhH}F_m$, and ${}^{PhX}_{PhH}F_p$, together constitute a complete specification of the influence of the substitutent group or atom X on the reactivity of the molecule C_6H_5X towards the reagent under consideration. For the substitution of nitrobenzene and chlorobenzene by the phenyl radical the relevant experimental values may be taken as :

	Rate ratio (Benzene = 1)	Isomerides, %: *ortho*	*meta*	*para*
Nitrobenzene	4·0	58	10	32
Chlorobenzene	1·44	62	24	14

which give rise to the following partial rate factors :

$${}^{Ph\cdot NO_2}_{PhH}F_o = 7{\cdot}0 \qquad {}^{Ph\cdot NO_2}_{PhH}F_m = 1{\cdot}2 \qquad {}^{Ph\cdot NO_2}_{PhH}F_p = 7{\cdot}9$$

$${}^{PhCl}_{PhH}F_o = 2{\cdot}7 \qquad {}^{PhCl}_{PhH}F_m = 1{\cdot}03 \qquad {}^{PhCl}_{PhH}F_p = 1{\cdot}2$$

Several attempts have been made to obtain a theoretical derivation of the directive influence of groups in heterolytic and homolytic aromatic substitution. From the figures given by Wheland [28] it is possible to calculate the partial rate factors for homolytic substitution in nitrobenzene and chlorobenzene; for nitrobenzene these are :

$${}^{Ph\cdot NO_2}_{PhH}F_o = 2{\cdot}25 \qquad {}^{Ph\cdot NO_2}_{PhH}F_m = 0{\cdot}85 \qquad {}^{Ph\cdot NO_2}_{PhH}F_p = 8{\cdot}7$$

Then, since $${}^{Ph\cdot NO_2}_{PhH}K = \tfrac{1}{6}\,(2\,{}^{Ph\cdot NO_2}_{PhH}F_o + 2\,{}^{Ph\cdot NO_2}_{PhH}F_m + {}^{Ph\cdot NO_2}_{PhH}F_p),$$

these partial rate factors lead to a value to 2·5 for ${}^{Ph\cdot NO_2}_{PhH}K$ for homolytic substitution without reference to the nature of the radical involved. In similar manner for chlorobenzene the calculated partial rate factors are :

$${}^{PhCl}_{PhH}F_o = 5{\cdot}8 \qquad {}^{PhCl}_{PhH}F_m = 1{\cdot}4 \qquad {}^{PhCl}_{PhH}F_p = 1{\cdot}9$$

from which ${}^{PhCl}_{PhH}K$ becomes 2·7, again without reference to the nature of the radical involved. Although numerical agreement is not close, the over-all picture is satisfactory in that it predicts predominant *o*/*p*-substitution in both nitrobenzene and chlorobenzene, and it also indicates mild activation in both cases. These results are the more remarkable since they are based on theoretical derivations made nearly ten years ago at a time when the experimental facts were unknown.

A new experimental method has been developed for the determination of partial rate factors which is *independent* of any knowledge of the proportions in which the isomerides are formed.[23] In this method, which is illustrated by application to the action of the phenyl radical on chlorobenzene, the assumption has to be made that the frequency factor, or the entropy of activation, remains constant throughout the series of reactions investigated, and that the energy contributions for the reaction at any one position in a polysubstituted benzene derivative are additive, or nearly so. This is not an unlikely assumption and is one for which there is some experimental support in the work of Ingold *et al.*[21] and in that of Bradfield and Brynmor Jones [29] on heterolytic substitution reactions of phenolic ethers. The experimental values required are the relative rates of substitution with reference to benzene for (*a*) chlorobenzene, (*b*) *p*-dichlorobenzene, and (*c*) *s*-trichlorobenzene. These were found to be :

$${}^{PhCl}_{PhH}K = 1{\cdot}44 \qquad {}^{p\text{-}C_6H_4Cl_2}_{PhH}K = 2{\cdot}69 \qquad {}^{s\text{-}C_6H_3Cl_3}_{PhH}K = 5{\cdot}02$$

which, for benzene = 6, become PhCl = 8·64, *p*-$C_6H_4Cl_2$ = 16·14, *s*-$C_6H_3Cl_3$ = 30·12. These values give rise to three equations involving three unknowns, which lead to a cubic equation in

any one of the three partial rate factors chosen. For the reaction with chlorobenzene we have :

$$8{\cdot}64 = 2F_o + 2F_m + F_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

For *p*-dichlorobenzene, in which there are four identical positions each influenced by one *o*- and one *m*-chlorine atom, we have :

$$4F_oF_m = 16{\cdot}14 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

whereas for *s*-trichlorobenzene, in which there are three identical positions each influenced by two *o*- and one *p*-chlorine atom, we have :

$$3F_o^2F_p = 30{\cdot}12 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

From (2) $F_m = 4{\cdot}035/F_o$ and from (3) $F_p = 10{\cdot}04/F_o^2$

Then $2F_o + 8{\cdot}07/F_o + 10{\cdot}04/F_o^2 = 8{\cdot}64$

therefore $2F_o^3 + 8{\cdot}07F_o + 10{\cdot}04 = 8{\cdot}64F_o^2$

i.e., $F_o^3 - 4{\cdot}32F_o^2 + 4{\cdot}035F_o + 5{\cdot}02 = 0$

The solution of this equation shows no real positive root, but if a relatively small allowance is made for experimental error and/or a slight divergence from the additive relationship on which the method is based, a positive root for ${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_o$ of 2·3 is obtained, which in turn gives ${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_m = 1{\cdot}75$ and ${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_p = 1{\cdot}9$.

The partial rate factors for homolytic substitution in chlorobenzene based on the three methods outlined above are summarised in Table 7. Each method indicates a predominance of substitution at the *o*- and *p*-positions, together with mild activation at all three positions. For purposes of comparison the partial rate factors for the nitration of chlorobenzene [25] are also included.

By means of the methods described above it has thus been possible to obtain for the first time a complete definition in quantitative terms of the influence of a substituent atom or group on a homolytic substitution reaction in the aromatic nucleus. It has been shown that both the nitro-group and the chlorine atom are *ortho-para*-directing substituents, the term being used in the conventional sense defined above, and that both substituents have an activating influence. The characteristic picture thus revealed is in close agreement with that obtained by theoretical

TABLE 7. *Partial rate factors for substitution in chlorobenzene.*

Reaction and method	${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_o$	${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_m$	${}^{\mathrm{PhCl}}_{\mathrm{PhH}}F_p$
Phenylation by infra-red analysis and competitive experiments	2·7	1·03	1·2
Calculation for Wheland's figures for homolytic substitution	5·8	1·4	1·9
Cubic method for phenylation	2·3	1·75	1·9
Nitration by HNO_3–Ac_2O	0·03	0·00	0·139

deduction. What has already been achieved with the nitro-group and the chlorine atom can be applied to other substituent groups or atoms, and in this way useful new information should result which will be of value in the wider fields of chemistry as a whole. The results so far obtained have a special personal significance in that they seem to provide a satisfactory, consistent, and rigid experimental vindication of some rather speculative ideas which were first put forward nearly 20 years ago.

It is customary on these occasions for the lecturer to thank those who have helped to contribute to the subject under discussion. In following precedent I do so not as a formal duty, but rather in a spirit of humble gratitude to all those who over many years have helped in this work. Their number is too large for me to mention all, but I should like to thank in particular my first collaborator, Dr. W. S. M. Grieve, who was with me at the start, and also my most recent collaborator, Dr. D. R. Augood, to whose skill and ability the success of much of the more recent work is very largely due. Finally, I place on record my special indebtedness to my colleagues at King's College, first to Dr. Gareth Williams, whose constant help has been invaluable, and then to Dr. W. C. Price and Dr. T. S. Robinson, who have provided us with expert advice and guidance in infra-red spectroscopy as well as with experimental facilities.

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OBITUARY NOTICES.

JAMES BADDILEY.

1885—1951.

JAMES BADDILEY, for many years director of research for the Dyestuffs Division of Imperial Chemical Industries Limited, died on September 26th, 1951, after an operation. Born on July 15th, 1885, at Blythe, Yorkshire, he was the eldest of a family of three sons and a daughter, his father being a well-known farmer and breeder of shire horses in the Worksop district. Baddiley received his early education at the Bradford Grammar School, proceeding in 1903 with a West Riding County scholarship to the Yorkshire College, Leeds, which became in the following year Leeds University. Here he was one of the first pupils of A. G. Green, who had been appointed to the Chair of Colour Chemistry and Dyeing the same year, and his success in Green's department determined his future career. Graduating in 1907 with first-class honours in Colour Chemistry, he was awarded the Le Blanc medal and also gained silver medals and first class certificates in the examinations of the City and Guilds Institute in both Coal Tar Products and Dyeing.

Green, with an established reputation for successful technical research and discoveries in the field of dyes, was now building a more academic research school at the University and it was natural that so promising a pupil as Baddiley should be invited to join him. This he did, and for the next two years he collaborated in investigations concerned with stilbene derivatives and the cotton dyes derived from them. His part was to study the action of alkali hydroxides on derivatives of *p*-nitrotoluene having substitutents in the *ortho*-position, in the course of which he prepared and examined many new derivatives of 4 : 4′-dinitrostilbene. The results of this work were published in a joint paper (Green and Baddiley, *J.*, 1908, **93**, 1721).

Leaving the University in 1909, Baddiley joined the firm of Levinstein Ltd. at Blackley, Manchester, where he was destined to remain for the whole of his industrial life. The first recruit to join this firm from Green's school at Leeds, he started as private assistant to Dr. Herbert Levinstein. Speaking of Baddiley at this time, Dr. Levinstein says: "He was a neat manipulator, a most pleasant person of good manners, good tempered, and easy to get on with. I was delighted with him and we did a good deal of work together with equal satisfaction, I think, to both of us." This description fitted well the man as we knew him later. He had an extraordinary fund of patience, whether in the progress of a research or the development of a policy and would never be rushed into a course until he was sure of his ground. He could at the same time be obstinate in his opinions when he believed he was right.

The years from the time he joined Levinstein's to 1914 were, as it transpired, a training period for his life's work, in which he was to play a leading part in the renaissance of the dyestuff industry in Britain. At Levinstein's, during the period of eclipse of the British industry, competition with the German firms had always been kept alive and the lamp of research had never been extinguished even if it had burnt low. Baddiley's work was mainly concerned with cotton dyes. At this time the use of derivatives of J acid (2-amino-5-naphthol-7-sulphonic acid) as components for azo-dyes, to confer cotton substantivity, was being developed in Germany and the identification by Baddiley of a Bayer product called Benzo Fast Red 8BL as a dye formed by coupling diazotised aminoazobenzenesulphonic acid with benzoyl-J acid led Levinstein and Baddiley to investigate this field. They obtained a number of patents for the manufacture of derivatives of J acid and their use in azo-dyes (B.P. 11,877; 15,068; 15,070; 26,577/1910; 12,281/1911) and built up a successful range for manufacture. A new black dye for velvet, Vulcan Black G, was invented and much work was done in developing azo-dyes of a new type, to be after-treated on the fibre with formaldehyde to render them faster to washing. These dyes had resorcinol or *m*-aminophenol as end component which rendered them reactive to formaldehyde so that a more complex and less soluble compound was produced in the fibre (B.P. 27,525; 28,296/1912; 1435; 1436; 25,547; 28,569/1913; 8569/1914). This early work must have given Baddiley his life-long interest in cotton substantivity and its relation to molecular size and solubility, a problem which at a later stage in his career recurred in connection with the dyeing of artificial fibres.

On the outbreak of war in 1914 it soon became most unpleasantly clear how far the British textile industry and other colour-using industries had become dependent on foreign, especially German, dyes. Prices of such stocks of dyes and intermediates as were in the country rose to

fantastic heights. The small dye-making firms, of which Levinstein's was one of the foremost, had forthwith to manufacture as fast as they could such dyes as were within their range and at the same time to do their best to discover as quickly as possible how to make a vast number of intermediates and dyes which had only been obtainable from abroad. Ivan Levinstein and his son at once started to build up a research department around Baddiley, with the assistance of A. G. Green who resigned his chair at Leeds and went to Manchester to found a school of dye research at the College of Technology whilst at the same time acting as adviser to Levinstein's. By early 1917, when the writer joined Baddiley, he had a staff of about 15 chemists engaged in working out processes for the manufacture of a wide range of benzene and naphthalene intermediates and of azo-, triarylmethane, and rhodamine dyes. Most of the staff were trying to keep several lines of research going at the same time, for the call for more manufacture was insistent. Baddiley, always ahead of his team in knowledge, experience, and wisdom, was there at hand to guide and advise. When the war came to an end the staff rapidly increased in numbers and for a time its supervision was divided between Baddiley and Green, the former being responsible for immediate technological problems, the latter for longer-range projects. In practice, however, there was little difference between the work and outlook of the two divisions and, in course of time, after Green's retirement, Baddiley became entirely responsible for all research. The amalgamation of Levinstein's with the Government-sponsored firm of British Dyes Ltd. and later the absorption of Scottish Dyes Ltd. into the British Dyestuffs Corporation brought Baddiley added responsibilities and more scope. Following the end of the war were several very difficult years, in which the national necessity for building up an efficient dyestuff industry was hard to reconcile with the need of the consumers, especially the textile industry, for a full range of dyes at the lowest possible prices. That the purely technical side of this obstinate problem was solved was largely due to the untiring work of Baddiley backed by his loyal research department, encouraged administratively by Dr. C. J. T. Cronshaw and supported by the then chief colourist, the late R. S. Horsfall, who was unfailing in his efforts to raise the standard of the Company's products. The technical progress of the industry made the satisfactory political solution of the dyestuffs problem possible. When the great chemical combine, Imperial Chemical Industries Limited, was formed in 1926, the British Dyestuffs Corporation was included and Baddiley's position as head of the Research Department of the Dyestuffs Group (afterwards Dyestuffs Division) was confirmed. In 1930 he became a Delegate Director of the Group and Joint Technical Manager, and he remained director in charge of research until his retirement in 1947.

Baddiley had few equals in his wide knowledge of the chemistry and technology of dyestuffs, backed as it was by a sound knowledge of organic chemistry and appreciation of its possibilities, and supported by a retentive memory. Necessarily most of his energy had to be devoted for many years to what became known as " imitative " work, the production of the equivalents of competitive continental dyes, but when the back of this work had been broken his department was able to devote more and more of its time and man-power to speculative and fundamental work on dyes and to other fields of applied organic chemistry. He always kept pace with these expanding interests and used his powers to great effect in developing chemicals for use as dyeing assistants and later in directing research in the fields of plastics, pest control products, and finally medicinal chemicals. His personal contributions were important and his name is associated with about fifty patents in the period 1915—1930. He paid particular attention to the problems of dyeing artificial fibres, including viscose (regenerated cellulose) and acetate rayon. It was at one time difficult to dye viscose rayon in level shades with direct cotton dyes, partly, no doubt, because of a certain lack of uniformity in the manufactured fibre. Associating this behaviour with a greater avidity of regenerated cellulose, compared with cotton, for direct dyes, Baddiley and his colleagues, P. Chorley and R. Brightman, invented a range of dyes having lower affinity for cotton but which yet dyed viscose satisfactorily, more slowly but in level shades. Many of these dyes contained gamma acid (2-amino-6-naphthol-8-sulphonic acid), in place of the isomeric J acid as a component (see B.P. 270,446 and additions, B.P. 277,756, 281,410, etc.). From these inventions came the Icyl range of dyes for viscose.

Baddiley's most noteworthy contribution to the dyeing of artificial fibres related, however, to the dyeing of acetate rayon. When a satisfactory cellulose acetate fibre had been produced by Dr. H. Dreyfus it was found that only a very few of the existing textile colouring matters would dye it and these few provided a hopelessly restricted range which could not be used together and had poor fastness properties. In general, solubility of a dye in water was incompatible with affinity for cellulose acetate. Baddiley has attributed the suggestion to colour the rayon by means of aqueous dispersions of insoluble, weakly basic coloured substances to two of

his colleagues, Horsfall and Sanderson. This suggestion led at first to the discovery only of a few yellow and orange dyes, but the outlook for the fibre was entirely changed when Baddiley with the late A. Sheperdson discovered that amino-derivatives of anthraquinone when applied from a dispersion had a strong affinity for acetate rayon, giving deep dyeings of a high degree of fastness. This basic discovery immediately opened a wide field, since it is possible by devices well known to the chemist to synthesise compounds from anthraquinone, containing one, two, or more simple or substituted amino-groups, of almost any colour in the spectrum. From this discovery came the important Duranol range of acetate dyes (B.P. 211,720). The fundamental value of this discovery was publicly recognised in 1939 by the Society of Dyers and Colourists by the award to Baddiley for this and his other great services to the dyestuff industry of its highest honour, the Perkin medal. He thus joined the ranks of a very distinguished company which includes such eminent chemists as Graebe, Liebermann, A. von Baeyer, and R. E. Schmidt amongst foreigners and A. G. Green and C. F. Cross amongst fellow-countrymen. On the occasion of the presentation of the medal Baddiley delivered a fascinating address on " Post-war Development in the Dyestuffs Industry " on which he could speak with the full authority of one who had taken a leading part therein (*J. Soc. Dyers and Col.*, 1939, **55**, 236).

In his earlier years Baddiley was a great walker and lover of the countryside and later a keen motorist, but he allowed few outside interests to interfere with his devotion to chemistry. Family connections ensured that he had a lively interest in the problems of agriculture and in the applications of chemistry to their solution. His intimate knowledge of the history and development of the German dye industry convinced him that the finest nursery for an organic chemist, whatever his ultimate destination, was a dyestuffs laboratory and he was happy to see successful research in other fields emanating from the laboratories under his charge. After his retirement he continued to attend research discussions at Blackley, maintaining his chemical interests to the end.

Baddiley took an enlightened view of the interdependence of pure and applied science and their need for one another's help. Under his régime the doors at Blackley were wide open to academic scientists, to numbers of whom he became a familiar figure. But for this he would have been little known to the chemical world outside the industry, for he was of a retiring disposition and shunned any kind of publicity. He always retained an affection for the University of Leeds, becoming in 1944 a member of its Textile and Dyeing Advisory Committee and in 1945 a life member of the University Court.

He married in 1915 Ivy Logan Cato and had four children, two sons and two daughters. One of his sons became a farmer, the other has already made his mark in the chemical profession, of which his father was so bright an ornament and so devoted a member.

E. H. Rodd.

SAMUEL SUGDEN *

1892—1950

Samuel Sugden was born in Leeds, Yorkshire, in 1892; he was the eldest son of a Samuel Sugden who was connected with wool trade journals.

He gained his secondary education at Batley Grammar School, where apparently he developed a very definite interest in science though, so far as can be ascertained, this did not come from any family bias or tradition. He won a Royal Scholarship, offered by the Board of Education, which took him to the Royal College of Science in London in October 1912. He had already passed the Intermediate Examination, so he was able to take the Final one in July 1914. On the result, he was awarded the Associateship of the Royal College of Science in chemistry, with First-Class Honours, and also the Governors' Prize for the best student in practical chemistry and the Frank Hatton Prize for proficiency in advanced chemistry. He showed himself to have not only outstanding ability but also very definite personality. He gave a memorable impression of energy and of extreme enthusiasm for the latest developments in science, not only by his liveliness in discussion but by his activity in doing such things as building wireless sets, a hobby which, in those days, was a most exciting form of pioneering.

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Sugden enjoyed his time at the Royal College of Science, though he had to tolerate a full share of chaff and banter, for he was a Yorkshireman with rough edges, and he was small of stature. Fortunately he had a very cheerful disposition and was not easily ruffled, so he took all this with good grace, and responded with gusto but without acrimony. He showed little interest in any form of sport, but he had one Yorkshire heritage—a love of choral music. This was, perhaps, accentuated by his having been brought up as a Wesleyan Methodist and being accustomed, therefore, to a high standard of congregational singing.

It was understood at the College that he had intended to stay there to do research in inorganic chemistry; but the outbreak of war in August 1914 appears to have caused him to change his plans. He left the College on October 6th, and first took employment as a chemist with a cement-manufacturing firm at Snodland, Kent. However, his strong sense of duty soon caused him to consider enlisting, so he made inquiries about obtaining a commission. In this he was unsuccessful, presumably because of his lack of inches; and in September 1915 he joined the Royal Army Medical Corps as a private soldier. He was soon disillusioned, for he was set to do bacteriological testing; and although his scientific training fitted him for this, the task quickly became a dull routine.

In June 1916 he was released to join the Research Department of the Royal Arsenal, Woolwich, as a chemist to work under the late Sir Robert Robertson, F.R.S. There he was much happier once he had recovered the ability to think, which process of convalescence, he said to a colleague, took fully three months. Although it is not possible to associate his name with any major discovery of that war, his work was of considerable importance in promoting the satisfactory performance of many munitions. It bore on the physical changes which took place in certain explosives during storage, and the devising of precautions essential during manufacture and filling to ensure correct functioning. He also developed methods for determining the specific surface of fine powders used as ingredient of certain explosives; and he developed smoke shells for ranging. In the latter connexion a colleague tells a story of how Sugden ingeniously contrived to make a pitch filling pulverize on explosion, by adding powdered charcoal, but how, in his instructions to the Ordnance Factory, he unfortunately omitted to specify that the charcoal should be powdered, so he received an urgent message that the charcoal sticks would not dissolve.

Out of the group of about a hundred scientists he found plenty of kindred spirits who would join him in lively discussions on any scientific topic that happened to arise. Nevertheless, he decided that the restraints of a Government scientific department were such that he would be happier in the academic world; so at the end of the war, as soon as he could, he sought a post; and on April 30th, 1919, he resigned from the Research Department to become a lecturer at Birkbeck College. Even during the war he actively pursued his interest in pure science, for in February 1917 he was elected a Fellow of the Chemical Society; and in 1918 he was awarded the external B.Sc. Degree of the University of London with First-Class Honours in Chemistry.

He undertook his new duties with great vigour, enthusiasm, and joy. He had found his vocation at last; and he very quickly made his mark, as will appear later. In passing it may be mentioned that he completed his academic qualifications by taking his M.Sc. Degree in 1921, and his D.Sc. Degree in 1924.

For a number of years he lived a cheerful, self-sufficient bachelor's life, running a small flat, and managing his domestic affairs very well. Quite suddenly, however, he surprised his friends by announcing his intention to marry; and in 1926 he married Eleanor, daughter of the late Thomas Dunlop of Glasgow.

He steadily accumulated advancement and honours. In 1928 he was appointed Reader in Physical Chenistry at Birkbeck College; and in the same year he became a Member of the Council of the Chemical Society. In 1932 he was appointed Professor of Physical Chemistry at the College and, again in the same year, he was elected an Honorary Secretary of the Chemical Society. In 1934 he was elected a Fellow of the Royal Society. In 1937, on the retirement of Professor F. G. Donnan, F.R.S., he was appointed a Professor of Chemistry at University College, London.

First at Birkbeck College, then at University College, Sugden established active schools of research, and also did much for the teaching of physical chemistry. He had wide scientific interests, independence, and originality, a gift for thorough analysis and for lucid exposition, great powers of self-discipline and concentration, and a very happy touch in personal relations. These qualities made him not only an excellent researcher and teacher, but also a good administrator in academic affairs.

Sugden was very sociable. He especially enjoyed entertaining his friends by his own fireside; and they found his company and that of his wife most refreshing. Not only did he have an impishness and a sly wit which were very attractive, but he had also a repertoire of stories appropriate to a wide variety of occasions. Sugden retained a certain amount of North Country cockiness; and to hear him engaging in a boasting match with one of his scientific colleagues was a most interesting experience. He was a redoubtable opponent for, if his adversary paused for breath, or for effect, Sugden, being small and nimble-witted, would quickly seize the initiative and talk him to a standstill. To younger scientists he was the kindest of persons: he never posed or tried to dominate, but unobtrusively made suggestions which were always shrewd and pertinent. He had definite views on politics; in his early days he was well to the Left, though subsequently he moved some way to the Right; but he was too interested in science to be a crusader.

The outbreak of the second war in 1939 brought an abrupt end to the comfortable phase in Sugden's life; indeed, as events turned out, it effectively ended his scientific career. In accordance with a previous arrangement he immediately joined the Ministry of Supply, and went to work at the Chemical Defence Experimental Station at Porton, near Salisbury. Although he had had no previous contact with this aspect of military science he threw himself into the work with so much vigour and good sense that he soon made substantial contributions. At first he was in charge of one particular practical problem, the elucidation of factors affecting the stability of certain war gases; but later he played a prominent part in the military assay of war gases, and particularly of new substances. Still later, he was for a time superintendent of the whole research group at Porton. At no time, however, did he allow himself to become an arm-chair scientist; he retained a very lively interest in what was actually being done in the laboratories and in the Chemical Defence factories.

Moved by a feeling of desperate urgency, Sugden spared no effort to get things done as well or as fast as he thought they should be. It is not easy or simple to communicate this sense to a somewhat rigid organization: one result of his attempts was that he incurred some personal unpopularity, and began to acquire a reputation for impatience which had not previously been associated with him. During this period also he had cause to be anxious for his wife's health and safety. Despite these personal trials, his enthusiasm never flagged; and he drove himself regardless of possible consequences. In 1942, feeling that chemical warfare would not be employed and that he could be more useful in another department, Sugden sought and obtained a transfer to the Armament Research Department. He was appointed Superintendent of Explosives Research on October 12th, 1942. Here again, however, he ran into difficulties; so in June 1943 he resigned, and soon after became Scientific Advisor to the U.S.A. 8th Army Air Force in Great Britain.

It speaks much for Sugden's devotion to his subject that at this time, despite all the cares and duties which distracted him, he accepted the invitation to give the Liversidge Lecture to the Chemical Society; and on April 15th, 1943 he delivered a most interesting and stimulating talk on magnetochemistry. He had also continued to serve the Society by being a Vice-President from 1939 to 1942, as he did again later from 1946 to 1949.

In November 1943 he had a quite severe attack of influenza, and he returned to work before his doctor approved. Soon after, he had what proved to be a severe breakdown in health, from which he did not properly recover until the summer of 1944. He returned to his academic duties in September 1944, and soon was helping to cope with the difficult post-war problems of restoration which faced University College. Hardly had relatively normal conditions been restored, however, when it became clear that he was unlikely to reap much reward for his hard work. In 1948 he developed symptoms of angina pectoris. He continued his normal life as best he could, but, though the smile and the friendliness remained, the energy and most of the fire had gone for ever. At first he affected to make light of his complaint, but soon he could no longer do this. He faced the position bravely and with resignation, as did also his wife. He died on October 20th, 1950, aged only fifty-eight years. He is survived by his widow; there were no children.

After going to Birkbeck College, Sugden lost little time in starting research. He appears at this period to have explored more than one possible field, for his first paper " On reduction by metals in acid solutions, Part I ' (*Trans.*, 1921, **119**, 233) is about a topic entirely different from anything he worked on later, and it is in fact the last of its kind. His second paper (*ibid.*, p. 1483) is the first of the series on surface tension and derived properties which made his name. It deals with experimental methods of measuring this property, as do also the third and the

fifth (*Trans.*, 1922, **121**, 858; 1924, **125**, 27); and they illustrate very well many of the good qualities of Sugden's work, his grasp of the literature and the background, his thoroughness, exactness, and careful attention to detail both of theory and in practical work, and the general good sense which enabled him to see what was important and what was not. There is no clue in these papers to the motive which led him to study surface tension; but one of his friends tells how one day he found Sugden, long before he went to Birkbeck College, measuring the surface tension of a reddish liquid which, Sugden explained, was molten T.N.T.; so this property may have interested him for some time. At all events, in his published work Sugden first dealt very carefully with the methods of measurement (*Trans.*, 1921, **119**, 1483; 1922, **121**, 858; 1924, **125**, 32); then in 1924 (*Trans.*, **125**, 32) he considered relations between surface tension (γ) and temperature or some other temperature-sensitive functions, including particularly the McLeod relation between surface tension and density. Very soon after, in the same year, he considered and rejected, on new evidence, the Langmuir and Harkins theory that surface tension is determined largely by the orientation of molecules in the surface (*ibid.*, p. 1168); and so he cleared the way for the formulation of the *parachor* (*ibid.*, p. 1177), *i.e.*, the function

$$P = \frac{M\gamma^{1/4}}{D - d}$$

where M is the molecular weight of the substance, γ is the surface tension of it as a liquid, and D and d are the densities, at the temperature of measurement of γ, of the liquid and the saturated vapour respectively. It is a function which, in effect, permits molecular volumes to be compared at the same internal pressure. It shows remarkable additivity, but there are several structural constants which have made possible attempts to answer structural problems which had been left unanswered or in doubt by the classical methods of organic and inorganic chemistry. From the three-year gap between his first paper on surface tension and the discovery of the parachor it seems unlikely that Sugden had at first a clear idea of where he was going, but rather that he was feeling his way and hoping that something would turn up. As soon as something did, he exploited it very ably.

From 1924 to 1932 he gave the greater part of his energy to applying the function, to considering its significance, or to searching for other useful molecular-volume functions. He published twenty-two papers on these topics (*J.*, 1924—1932). The best idea of the work is obtained from his book "The Parachor and Valency," published in 1930, which surveys all the papers save the last few, and adds considerably to them. It is an admirable work in many ways.

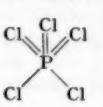
All the initial applications turned upon two constitutional constants, one for the degree of unsaturation and the other for the presence of a semipolar double bond, or dative link. The degree of unsaturation was defined as x/n, where x is the number of latent valencies, or the number of hydrogen atoms needed to give saturation, and n is the number of atoms in the ring—which may be two or more. This constitutional constant is then $23{\cdot}2x/n$. Thus a double bond gives an increment of 23·2; but a six-membered ring gives one of only 7·7. The constant for the semipolar double bond is $-1{\cdot}6$.

These constants could not be predicted theoretically any more than could those for the atoms; but the unsaturation expression was based on experimental values for rings which had been established by standard organic chemical arguments; and the semipolar double bond value was derived from compounds which were supposed to have this bond in order to conserve the valency group of eight postulated by G. N. Lewis, *e.g.*, nitro-compounds.

On this basis Sugden was able to choose between alternative formulæ for several organic compounds, which differed according to whether there were multiple links or rings, or chains; *e.g.*, he showed that paraldehyde has a ring rather than a chain structure, that benzoquinone is a monocyclic diketone rather than a trans-annular peroxide, and that benzil is a chain and not a ring compound; he supported Ott's and Pfeiffer's views (*Ber.*, 1922, **55**, 413) about the structures of the two forms of phthaloyl chloride. He also examined some examples of ring–chain tautomerism, and found qualitative support for Ingold and Shoppee's conclusions (*J.*, 1928, 365, 1662, 1868) regarding the phorones, though there were anomalies which prevented a quantitative analysis of the problem from being made.

He showed that the observed parachors are consistent with Lowry's hypothesis that when the higher valencies of elements such as phosphorus or sulphur are developed by the attachment of oxygen, the new bonds are semipolar double bonds and not ordinary double bonds. This agreed with current theory and with current interpretation of the stereochemical evidence, but it was regarded as a striking and valuable confirmation thereof. Sugden developed his

thesis much farther, however, for he concluded on similar grounds that whenever the co-ordination number exceeds four, some of the atoms or groups are attached by one-electron or " singlet " links, as, for example, in phosphorus pentachloride, following an earlier suggestion by Prideaux; and also that in chelate rings the links between the metal atom and what is nowadays called the ligand are singlet ones. He proposed singlet linkages in a number of other complex compounds, and developed a coherent theory that they were formed (*a*) whenever the valency group would otherwise exceed eight, or (*b*) because duplet bonds would give anomalous charge distributions, as, for example, in the aluminium derivative acetylacetone wherein the dative links, if each were supposed to give a transfer of one electron charge, would give a negative charge of three units to the metal atom; and he concluded that a singlet link is more stable when it joins two elements which differ markedly in their electron affinity. His views were criticized by Sidgwick (" Electronic Theory of Valency," Oxford, 1927, Chapter VII), who pointed out that many of the parachor results could be explained on duplet formulæ if it be supposed that there is a negative parachor value corresponding to the expansion of a valency group beyond an octet.



Sugden argued (with Waloff, *J.*, 1932, 1492), however, that the only consistent alternative would be to assume that the sharing of each extra electron (*i.e.*, over and above the number for which the normal parachor constants are derived) would cause a contraction of 11·6 units; and he showed that there is no such change when the number of electrons shared by an atom is altered, as in some series of mercury, thallium, and boron compounds. It is certainly true that the singlet link hypothesis provides a remarkably consistent interpretation of parachor values, though inspection of some of the numerical data shows that there are minor discrepancies; and it formally solves the difficulty of the improbable charges in the duplet formulation of complex compounds. Anomalies were found, however; *e.g.*, it was shown that some of the thallium compounds on which his argument rested are actually associated to definite degrees in solution (Sidgwick and Sutton, *J.*, 1930, 1461), and that some non-associated *o*-substituted phenols which might be supposed to have a chelate ring involving a hydrogen bond, show an anomaly which does not correspond to singlet linkages (Sidgwick and Bayliss, *J.*, 1930, 2027). Furthermore, considerable doubts were expressed as to whether such a singlet link would have the strength, compared with that of duplet links, which the chemical facts require. This last criticism was made very pointedly in 1931 by Pauling (*J. Amer. Chem. Soc.*, 1931, **53**, 3229) who, in the course of a systematic application of wave mechanics to the problems of chemical binding, concluded that singlet electron links would be only about half or two-thirds as strong as duplet links, and that they were likely to be formed only between atoms of equal or nearly equal electron affinity. Sugden's theories on this matter were thereafter largely discounted, and he himself eventually abandoned them, though he retained a sentimental regard for the singlet link.

In looking back at this old controversy one sees that it came at the end of an era when structural investigations by physicochemical means as we know them now were all but impossible. After the molecular weight of a substance had been determined, the only further steps which could be taken were to measure its boiling point and its solubility, and perhaps to determine its molecular refractivity; and then to speculate on the basis of a very primitive theory. The discovery of a new property which might give information about structure was therefore an important event; and it had the very valuable indirect effect of prompting chemists to search for other such properties. In retrospect it is clear that the parachor was not a satisfactory property for the analysis of structure because its value as a function thereof could not be predicted with certainty on a basis of physical theory. This meant, and still does, that predictions were based essentially on numerical consistency and on bold assumptions of analogy, which bases proved ambiguous or inadequate. The parachor led, in fact, to the wrong conclusion about the structure of the azides; and it did not give any clue to the mystery of the stability of benzene, for the observed parachor agreed well with that for a single Kekulé structure. Despite this, those who were working in the field at the time remember vividly how stimulating was Sugden's pioneer work, and know how much it did to help bring in the new era.

After 1930 there developed rapidly several other methods of examination which gave more direct information about molecular structure, and Sugden soon turned his attention to some of them. He first interested himself in the relation between magnetism and electronic structure. In this work he used experimental techniques and theoretical methods which had been developed by others, but he showed all his usual liveliness and perceptiveness in the choice of topics. He applied measurements of the paramagnetic moments of molecules to various ends. Thus he used them to investigate the electronic arrangement within metallic ions, either simple or

complex, and in neutral co-ordination compounds, and correlated this with the stereochemical arrangement of the co-ordinated groups [(with Morgan) *Nature*, **1931**, **128**, 31; *J.*, 1932, 161, 246; (with Barkworth) *Nature*, **1937**, **139**, 374; (with Nettleton) *Proc. Roy. Soc.*, 1939, *A*, **173**, 313; *J.*, **1943**, 328]. He also showed that certain organic molecules are paramagnetic and therefore are free radicals [(with Kenyon) *J.*, 1932, 161; *Trans. Faraday Soc.*, **1934**, **30**, 18; with Allen, *J.*, 1936, 440] but that hypophosphoric acid is not paramagnetic and therefore is $H_4P_2O_6$ and not H_2PO_3 [(with Bell) *J.*, **1933**, 48].

In connexion with the first topic, he prepared two isomeric nickel benzylmethylglyoximes [*J.*, 1932, 246; (with Cavell) *J.*, 1935, 621], which indicated the possibility of *cis–trans*-isomerism, and therefore that the four nickel valencies are directed to the corners of a square. This possibility had been predicted by Pauling and, furthermore, according to his theory both of them should be diamagnetic. Sugden showed that in fact they are. He went on to examine a number of cobalt complexes, and showed that the quenching of the orbital component is far from complete and that it depends in some way upon the nature of the ligand. In his Liversidge lecture (*J.*, **1943**, 328) he gave a most excellent critical discussion of such matters. Among his last papers was a series on the magnetic susceptibility of the rare-earth elements [*J.*, 1949, (with Hilal) 135 and (with Tailby) 136, 137, 139].

Soon after he became actively interested in magnetic measurements Sugden started work also on dielectric measurements (*J.*, **1933**, 768; *Nature*, **1934**, **133**, 415). He showed that the electric dipole moments of substituted nickel glyoximes give some support to the hypothesis that they exist as *cis–trans*-isomers (with Cavell, *loc. cit.*); but his major contributions in this field came from measurements of electric moments in the gas phase. In the course of a series of systematic investigations [(with Groves) *J.*, 1934, 1094; 1935, 971; 1937, 158, 1779, 1782, 1992; also *Trans. Faraday Soc.*, **1934**, **30**, 734] he gave careful attention to the question of the magnitude of atom polarizations and to the best way of allowing for them. He became convinced, also, of the importance of making a more complete and general allowance than hitherto for the alteration of the moments of whole molecules by inductions between the component moments; so he set about this difficult task, and thus obtained a new set of bond moments. By means of these he was able, for example, to confirm the existence of anomalies in benzene derivatives which had been previously noticed and correlated with the " electron drifts " postulated by organic chemists in their theories of reaction.

Sugden's other major scientific interest was the use of radioactive tracer elements in chemistry. He did some useful work on the technique of concentrating the radio-bromine formed by neutron bombardment [(with Le Roux and Lu), *Nature*, 1939, **143**, 517; (with Lu) *J.*, 1939, 1273], and then proceeded to use this element for studying the changes in the parameters of the reaction $RBr + Br^{*-} \longrightarrow RBr^{*} + Br^{-}$, with variations of R and of solvent [*J.*, 1939, (with Le Roux) 1279, (with Elliott) 1836; (with Le Roux, Lu, and Thomson) 1945, 586; (with Evans) 1949, 270]. This work was interrupted by the 1939—1945 war, but even so he obtained a number of results which began to form a pattern and which revealed the surprising fact that the slowness of the reaction of bromo-2 : 4-dinitrobenzene, relative to that of alkyl bromides, is due not to a high activation energy but to a low effective collision area.

Besides his major book, " The Parachor and Valency," Sugden translated, from the German, Alfred Stock's book on " The Structure of Atoms " (1923), and, in conjunction with the late Professor T. Martin Lowry, F.R.S., he wrote the well-known textbook " A Classbook in Physical Chemistry "(1929).

In appraising Sugden's work, it must be remembered that his working life, as an academic scientist, was little more than the twenty years of the last peace, for after the war he had hardly been able to do more than start research again before he was stricken by illness. In that time he was remarkably productive. He was, indeed, one of the most galvanic figures among English chemists. He was very versatile; and, because of his originality and thoroughness, he added much to every subject he touched.

He will be remembered by his many friends not only for his intellectual gifts, his kindness, and his personal courage, but for his zest. He really enjoyed learning and research; and he had the power of communicating that joy to others.

L. E. Sutton.

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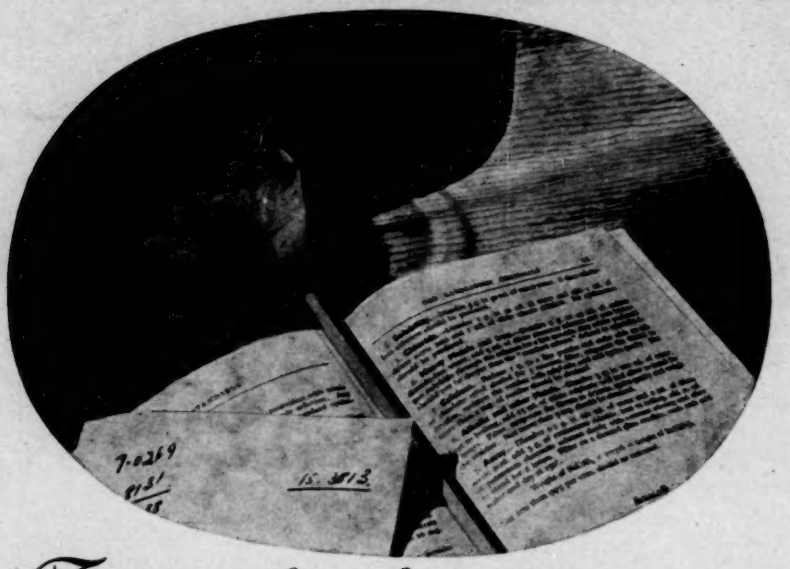

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